

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	6	glnap\$8	USPAT; US-PGPUB	2003/06/17 14:01
2	L2	331546	acetyl adj phosphate or acetylphosphate or acetate	USPAT; US-PGPUB	2003/06/17 14:02
3	L3	76345	promoter\$1	USPAT; US-PGPUB	2003/06/17 14:02
4	L4	1383639	induc\$8 or regulat\$8 or activat\$8 or modulat\$8	USPAT; US-PGPUB	2003/06/17 14:02
5	L5	60	2 near10 4 near10 3	USPAT; US-PGPUB	2003/06/17 14:03
6	L6	9302	pps or phosphoenol adj pyruvate adj synthase\$1	USPAT; US-PGPUB	2003/06/17 14:29
7	L7	94	6 near4 (gene\$1 or sequence\$1)	USPAT; US-PGPUB	2003/06/17 14:29
8	L8	22	7 same (overexpress\$ or amplif\$10 or increas\$8)	USPAT; US-PGPUB	2003/06/17 14:30
9	L9	17	7 and 2	USPAT; US-PGPUB	2003/06/17 14:48
10	L10	6285	lycopene\$1 or isoprenoid\$1 or carotene\$1 or astaxanthin\$1	USPAT; US-PGPUB	2003/06/17 14:58
11	L11	1	6 same 10	USPAT; US-PGPUB	2003/06/17 14:58
12	L12	1563	6 and 2	USPAT; US-PGPUB	2003/06/17 15:01
13	L13	1563	12 and 6	USPAT; US-PGPUB	2003/06/17 15:01
14	L14	3593	10 and 2	USPAT; US-PGPUB	2003/06/17 15:01
15	L15	9	14 and 6	USPAT; US-PGPUB	2003/06/17 15:01

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	6	glnap\$8	USPAT; US-PGPUB	2003/06/17 14:01
2	L2	331546	acetyl adj phosphate or acetylphosphate or acetate	USPAT; US-PGPUB	2003/06/17 14:02
3	L3	76345	promoter\$1	USPAT; US-PGPUB	2003/06/17 14:02
4	L4	1383639	induc\$8 or regulat\$8 or activat\$8 or modulat\$8	USPAT; US-PGPUB	2003/06/17 14:02
5	L5	60	2 near10 4 near10 3	USPAT; US-PGPUB	2003/06/17 14:03

PGPUB-DOCUMENT-NUMBER: 20030108986

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030108986 A1

TITLE: Compositions and methods comprising G-protein coupled  
receptors

PUBLICATION-DATE: June 12, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Communi, Didier	Dilbeek		BE	
Lannoy, Vincent	Brussels		BE	
Brezillon, Stephane	Brussels		BE	
Detheux, Michel	Mons		BE	
Parmentier, Marc	Brussels		BE	
Govaerts, Cedric	Brussels		BE	

APPL-NO: 10/ 079384

DATE FILED: February 20, 2002

RELATED-US-APPL-DATA:

child 10079384 A1 20020220

parent continuation-in-part-of 09885453 20010621 US PENDING

US-CL-CURRENT: 435/69.1, 435/320.1, 435/325, 435/7.1, 530/350, 536/23.5  
, 800/8

ABSTRACT:

The present invention relates to G-protein coupled receptors and the nucleic acid molecules encoding them. The invention further relates to methods of screening for compounds which modulate the activity of one or more of the G-protein coupled receptors disclosed herein, and methods for modulating receptor activity. The invention also provides a natural ligand for one or more of the G-protein coupled receptors disclosed herein, and methods for identifying other natural ligands for these receptors.

RELATED APPLICATION

[0001] This application claims priority under 35 U.S.C. .sctn.120 to U.S. application Ser. No. 09/885,453, filed Jun. 20, 2001, which is incorporated herein by reference in its entirety.

----- KWIC -----

Detail Description Paragraph - DETX (113):

[0238] Additional examples of transcriptional control elements that are responsive to changes in GPCR activity include, but are not limited to those responsive to the AP-1 transcription factor and those responsive to NF- $\kappa$ B activity. The consensus AP-1 binding site is the palindrome TGA(C/G)TCA (Lee et al., 1987, Nature 325: 368-372; Lee et al., 1987, Cell 49: 741-752). The AP-1 site is also responsible for mediating induction by tumor promoters such as the phorbol ester 12-O-tetradecanoylphorbol-beta.-acetate (TPA), and are therefore sometimes also referred to as a TRE, for TPA-response element. AP-1 activates numerous genes that are involved in the early response of cells to growth stimuli. Examples of AP-1-responsive genes include, but are not limited to the genes for Fos and Jun (which proteins themselves make up AP-1 activity), Fos-related antigens (Fra) 1 and 2, I $\kappa$ B $\alpha$ , ornithine decarboxylase, and annexins I and II.



PGPUB-DOCUMENT-NUMBER: 20030104478

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030104478 A1

TITLE: Natural ligand of G protein coupled receptor ChemR23  
and uses thereof

PUBLICATION-DATE: June 5, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Wittamer, Valerie	Waterloo		BE	
Communi, David	Braine le Chateau		BE	
Vandenbogaerde, Ann	Munchen		DE	
Detheux, Michel	Mons		BE	
Parmentier, Marc	Beersel		BE	

APPL-NO: 10/ 201187

DATE FILED: July 23, 2002

RELATED-US-APPL-DATA:

child 10201187 A1 20020723

parent continuation-of PCT/EP02/07647 20020709 US UNKNOWN

child 10201187 A1 20020723

parent continuation-in-part-of 09905253 20010713 US PENDING

non-provisional-of-provisional 60303858 20010709 US

US-CL-CURRENT: 435/7.1

ABSTRACT:

The present invention relates to a G-protein coupled receptor and a novel ligand therefor. The invention provides screening assays for the identification of candidate compounds which modulate the activity of the G-protein coupled receptor, as well as assays useful for the diagnosis of a disease or disorder related to the dysregulation of G-protein coupled receptor signaling.

PRIORITY

[0001] This application claims priority under 35 U.S.C. .sctn.120 as a continuation in part of U.S. application Ser. No. 09/905,253, filed Jul. 13, 2001, which claims priority under 35 U.S.C. .sctn.119(e) to U.S. Provisional application No. 60/303,858, filed Jul. 9, 2001.

----- KWIC -----

Detail Description Paragraph - DETX (83):

[0178] Additional examples of transcriptional control elements that are responsive to changes in GPCR activity include, but are not limited to those responsive to the AP-1 transcription factor and those responsive to NF- $\kappa$ B activity. The consensus AP-1 binding site is the palindrome TGA(C/G)TCA (Lee et al., 1987, Nature 325: 368-372; Lee et al., 1987, Cell 49: 741-752). The AP-1 site is also responsible for mediating induction by tumor promoters such as the phorbol ester 12-O-tetradecanoylphorbol-beta-acetate (TPA), and are therefore sometimes also referred to as a TRE, for TPA-response element. AP-1 activates numerous genes that are involved in the early response of cells to growth stimuli. Examples of AP-1-responsive genes include, but are not limited to the genes for Fos and Jun (which proteins themselves make up AP-1 activity), Fos-related antigens (Fra) 1 and 2, I. $\kappa$ B.alpha., ornithine decarboxylase, and annexins I and II.

PGPUB-DOCUMENT-NUMBER: 20030104356

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030104356 A1

TITLE: Compounds and methods for treating and screening viral reactivation

PUBLICATION-DATE: June 5, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Berger, Shelly L.	Wayne	PA	US	

APPL-NO: 10/ 108164

DATE FILED: March 26, 2002

RELATED-US-APPL-DATA:

child 10108164 A1 20020326

parent continuation-of 09424348 19991122 US ABANDONED

US-CL-CURRENT: 435/5, 424/186.1

ABSTRACT:

This invention relates to host cellular factors as therapeutic and diagnostic compounds, and methods using such factors for screening for antiviral compounds, particularly compounds useful to treat Herpesvirus infections, such as HSV-1 and HSV-2 infections.

----- KWIC -----

Detail Description Paragraph - DETX (309):

[0287] Varnum, B. C., Lim, R. W. & Herschman, H. R. (1989).

Characterization of TIS7, a gene induced in Swiss 3T3 cells by the tumor promoter tetradecanoyl phorbol acetate. Oncogene 4, 1263-1265.

PGPUB-DOCUMENT-NUMBER: 20030096833

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030096833 A1

TITLE: Substituted indeno[1,2-c]isoquinoline derivatives and  
methods of use thereof

PUBLICATION-DATE: May 22, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Jagtap, Prakash G.	Beverly	MA	US	
Baloglu, Erkan	Boston	MA	US	
van Duzer, John H.	Georgetown	MA	US	
Szabo, Csaba	Gloucester	MA	US	
Salzman, Andrew L.	Belmont	MA	US	

APPL-NO: 09/ 944524

DATE FILED: August 31, 2001

US-CL-CURRENT: 514/285, 546/62 , 546/70

ABSTRACT:

The invention provides a novel class of substituted indeno[1,2-c]isoquinoline derivatives. Pharmaceutical compositions and methods of making and using the compounds, are also described.

----- KWIC -----

Summary of Invention Paragraph - BSTX (57):

[0053] The compositions may be sterilized and/or contain minor amounts of non-toxic adjuvants, such as preserving, stabilizing, wetting or emulsifying agents, solution **promoters, salts for regulating the osmotic pressure pH buffering agents, and other substances such as for example, sodium acetate,** triethanolamine oleate, etc. In addition, they may also contain other therapeutically valuable substances.

PGPUB-DOCUMENT-NUMBER: 20030096299

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030096299 A1

TITLE: Natural ligand of G protein coupled receptor ChemR23  
and uses thereof

PUBLICATION-DATE: May 22, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Wittamer, Valerie	Waterloo		BE	
Communi, David	Braine le Chateau		BE	
Vandenbogaerde, Ann	Munchen		DE	
Detheux, Michel	Mons		BE	
Parmentier, Marc	Linkebeek		BE	

APPL-NO: 09/ 905253

DATE FILED: July 13, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60303858 20010709 US

US-CL-CURRENT: 435/7.1

ABSTRACT:

The invention relates to the identification of TIG2, the polypeptide product of Tazarotene-Induced Gene 2, as a natural ligand of the ChemR23 G protein coupled receptor (GPCR). The invention encompasses the use of the interaction of ChemR23 polypeptides and TIG2 polypeptides as the basis of screening assays for agents that modulate the activity of the ChemR23 receptor. The invention also encompasses diagnostic assays based upon the ChemR23/TIG2 interaction, as well as kits for performing diagnostic and screening assays.

[0001] This application claims priority to U.S. Provisional No: \_\_\_\_\_, filed Jul. 19, 2001.

----- KWIC -----

Detail Description Paragraph - DETX (82):

[0171] Additional examples of transcriptional control elements that are responsive to changes in GPCR activity include, but are not limited to those responsive to the AP-1 transcription factor and those responsive to NF- $\kappa$ B activity. The consensus AP-1 binding site is the palindrome TGA(C/G)TCA (Lee

et al., 1987, Nature 325: 368-372; Lee et al., 1987, Cell 49: 741-752). The AP-1 site is also responsible for mediating induction by tumor promoters such as the phorbol ester 12-O-tetradecanoylphorbol-beta.-acetate (TPA), and are therefore sometimes also referred to as a TRE, for TPA-response element. AP-1 activates numerous genes that are involved in the early response of cells to growth stimuli. Examples of AP-1-responsive genes include, but are not limited to the genes for Fos and Jun (which proteins themselves make up AP-1 activity), Fos-related antigens (Fra) 1 and 2, I.kappa.B.alpha., ornithine decarboxylase, and annexins I and II.

PGPUB-DOCUMENT-NUMBER: 20030078212

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030078212 A1

TITLE: PHARMACEUTICAL COMPOSITIONS CONTAINING POLY(ADP-RIBOSE)  
GLYCOHYDROLASE INHIBITORS AND METHODS OF USING THE SAME

PUBLICATION-DATE: April 24, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
LI, JIA-HE	COCKEYSVILLE	MD	US	
ZHANG, JIE	ELLICOTT CITY	MD	US	

APPL-NO: 09/ 182645

DATE FILED: October 30, 1998

CONTINUED PROSECUTION APPLICATION: This is a publication of a continued prosecution application (CPA) filed under 37 CFR 1.53(d).

US-CL-CURRENT: 514/22, 514/25

ABSTRACT:

The present invention relates to pharmaceutical compositions containing poly(ADP-ribose) glucohydrolase inhibitors, also known as PARG inhibitors, and methods of using the same for inhibiting or decreasing free radical induced cellular energy depletion, cell damage, or cell death. More particularly, the present invention relates to pharmaceutical compositions containing poly(ADP-ribose) glucohydrolase inhibitors such as glucose derivatives; lignin glycosides; hydrolysable tannins including gallotannins and ellagitannins; adenoside derivatives; acridine derivatives including 6,9-diamino-2-ethoxyacridine lactate monohydrate; tilorone analogs including tilorone R10.556, daunomycin or daunorubicin hydrochloride; ellipticine; proflavine; and other PARG inhibitors; and their method of use in treating or preventing diseases or conditions due to free radical induced cellular energy depletion and/or tissue damage resulting from cell damage or death due to necrosis, apoptosis, or combinations thereof.

----- KWIC -----

Summary of Invention Paragraph - BSTX (29):

[0028] The use of the PARG inhibitor tannic acid for treating HIV infection is discussed in Uchiumi et al., "Inhibitory Effect of Tannic Acid on Human Immunodeficiency Virus **Promoter Activity Induced by 12-O-Tetra Decanoylphorbol-13-acetate** in Jurkat T-Cells", Biochem. Biophys. Res. Comm.

220:411-417 (1996).



PGPUB-DOCUMENT-NUMBER: 20030050235

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030050235 A1

TITLE: Natural ligand for orphan G protein coupled receptor  
GPR86 and methods of use

PUBLICATION-DATE: March 13, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Communi, Didier	Dilbeek		BE	
Suarez, Nathalie	Bruxelles		BE	
Detheux, Michel	Mons		BE	
Brezillion, Stephane	Bruxelles		BE	
Lannoy, Vincent	Liernu		BE	
Parmentier, Marc	Linebeek		BE	
Boeynaems, Jean-Marie	Wemmel		BE	

APPL-NO: 09/ 924125

DATE FILED: August 7, 2001

US-CL-CURRENT: 514/12, 435/7.21

ABSTRACT:

The present invention is related to a recombinant cell expressing a nucleotide sequence encoding a G protein coupled receptor having an amino acid sequence which presents more than 70% sequence identity with SEQ ID.NO.1 as well as to a drug screening method and kit using the orphan G protein coupled receptor GPR86, identified hereafter as receptor for ADP (P2Y.sub.13) and a homologous sequence, the corresponding polynucleotide and said recombinant cell to identify agonist, inverse agonist and antagonist compounds applicable to a diagnostic, prevention and/or treatment of various diseases and disorders.

----- KWIC -----

Detail Description Paragraph - DETX (112):

[0193] Additional examples of transcriptional control elements that are responsive to changes in GPCR activity include, but are not limited to those responsive to the AP-1 transcription factor and those responsive to NF- $\kappa$ B activity. The consensus AP-1 binding site is the palindrome TGA(C/G)TCA (Lee et al., 1987, Nature 325: 368-372; Lee et al., 1987, Cell 49: 741-752). The AP-1 site is also responsible for mediating induction by tumor promoters such as the phorbol ester 12-O-tetradecanoylphorbol-beta.-acetate (TPA), and are therefore sometimes also referred to as a TRE, for TPA-response element. AP-1

activates numerous genes that are involved in the early response of cells to growth stimuli. Examples of AP-1-responsive genes include, but are not limited to the genes for Fos and Jun (which proteins themselves make up AP-1 activity), Fos-related antigens (Fra) 1 and 2, I.kappa.B.alpha., ornithine decarboxylase, and annexins I and II.

PGPUB-DOCUMENT-NUMBER: 20020192262

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020192262 A1

TITLE: 1'-Acetoxychavicol acetate for tuberculosis treatment

PUBLICATION-DATE: December 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Palittapongampim, Prasit	Bangkok		TH	
Kirdmanee, Chalermpol	Bangkok		TH	
Kittakoop, Prasat	Prathumthani		TH	
Rukseree, Kamolchanok	Bangkok		TH	

APPL-NO: 10/ 152570

DATE FILED: May 23, 2002

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
TH	066318	2001TH-066318	June 18, 2001

US-CL-CURRENT: 424/422

ABSTRACT:

1'-Acetoxychavicol acetate is a compound not known before to possess anti-tuberculous activity. The above data revealed that the compound was active against the standard H37Ra strain as well as several clinical isolates at the concentration well below the toxic concentration against various mammalian cells. The compound is therefore potentially useful as an therapeutic and preventive agent for tuberculosis as well as an antiseptic agent against the bacteria.

----- KWIC -----

Detail Description Paragraph - DETX (31):

[0046] 8. Kondo, A., Ohigashi, H., Murakami, A., Suratwadee, J., and Koshimizu, K. 1'-Acetoxychavicol **acetate as a potent inhibitor of tumor-promoter-induced** Epstein-Barr virus activation from Languas galanga, a traditional Thai condiment. Biosci Biotechnol Biochem 1993;57:1344-1345.

US-PAT-NO: 6506598

DOCUMENT-IDENTIFIER: US 6506598 B1

\*\*See image for Certificate of Correction\*\*

TITLE: Cell culture process

DATE-ISSUED: January 14, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Andersen; Dana C.	Redwood City	CA	N/A	N/A
Bridges; Tiffany M.	Burlingame	CA	N/A	N/A
Gawlitsek; Martin	Foster City	CA	N/A	N/A
Hoy; Cynthia A.	Hillsborough	CA	N/A	N/A

APPL-NO: 09/ 553924

DATE FILED: April 21, 2000

PARENT-CASE:

This is a non-provisional application claiming priority to provisional application no. 60/131,076 , filed Apr. 26, 1999, the entire disclosure of which is hereby incorporated by reference.

US-CL-CURRENT: 435/359, 435/252.3 , 435/358 , 435/69.6 , 530/395

ABSTRACT:

A glycoprotein is produced by a process comprising culturing mammalian host cells expressing nucleic acid encoding said glycoprotein in the presence of (a) a factor that modifies growth state in a cell culture, (b) a divalent metal cation that can adopt and prefers an octahedral coordination geometry, and/or (c) a plasma component. In this process, the occupancy of an N-linked glycosylation site occupied only in a fraction of a glycoprotein is enhanced. Such culturing is preferably carried out at a temperature of between about 30.degree. C. and 35.degree. C. and/or in the presence of up to about 2 mM of a butyrate salt and/or in the presence of a cell-cycle inhibitor.

23 Claims, 16 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 8

----- KWIC -----

Detailed Description Text - DETX (14):

By "plasma component" is meant a constituent of normal plasma. This would include growth **promoters and tumor-promoting agents for endothelial cell growth, regulators of differentiation of epithelial tissues, glucagon, heparin, phorbol myristate acetate,** PRL, thyroglobulin, 8Br-cAMP, thrombin, vitamin A and its derivatives (retinoids such as retinoic acid, e.g., beta-all-trans retinoic acid), glutathione, steroids such as corticosterone, cortisol, and corticoids, e.g., glucocorticoids such as hydrocortisone, and hormones, preferably those that are vital hormones of metabolism such as estrogen, insulin, and thyroid hormones, e.g., thyroxine and tri-iodothyronine (T.sub.3). The thyroid hormones are preferred, and most preferably thyroxine and tri-iodothyronine. Since some serum, including fetal calf serum, contains thyroid hormones and the thyroid hormone binding protein at nanomolar levels, it is preferred to use serum-free medium, particularly if thyroid hormones are employed to enhance site-occupancy.

US-PAT-NO: 6504048

DOCUMENT-IDENTIFIER: US 6504048 B1

TITLE: Flavorant compositions

DATE-ISSUED: January 7, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bachmann; Jean-Pierre	Wadenswil	N/A	N/A	CH
Gautschi; Markus	Zeiningen	N/A	N/A	CH
Hostettler; Bernhard	Gockhausen	N/A	N/A	CH
Yang; Xiaogeng	West Chester	OH	N/A	N/A

APPL-NO: 09/ 634029

DATE FILED: August 8, 2000

PARENT-CASE:

This is a Continuation Application of U.S. application Ser. No. 09/212,985, now Pat. No. 6,203,839 filed Dec. 16, 1998, now Pat. No. 6,203,839 which is incorporated herein by reference in its entirety. This application is also related to application Ser. No. 09/634,067, filed on even date herewith and entitled "Flavorant Compositions", and is incorporated herein by reference in its entirety.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
EP	97122633	December 22, 1997

US-CL-CURRENT: 560/254, 426/533 , 426/538 , 426/546 , 560/221

ABSTRACT:

The invention is related to a flavorant composition containing 1'-acetoxychavicol acetate and 1'-acetoxyeugenol acetate derivatives thereof as well as a flavorant acceptable carrier. The flavorant composition may be used for flavoring foods, beverages or healthcare products with warm/hot, spicy and pungent sensations related to Galangal.

15 Claims, 0 Drawing figures

Exemplary Claim Number: 1

----- KWIC -----

Other Reference Publication - OREF (8):

Kondo, et al., 1'Acetoxychavicol **Acetate as a Potent Inhibitor of Tumor Promoter-induced** Epstein-Barr Virus Activation from *Lanquas galanga*, a Traditional Thai Condiment, Biosci. Biotech. Biochem. 57(8) (1993) 1344-1345.

US-PAT-NO: 6476252

DOCUMENT-IDENTIFIER: US 6476252 B1

TITLE: Flavorant compositions

DATE-ISSUED: November 5, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bachmann; Jean-Pierre	Wadenswil	N/A	N/A	CH
Gautschi; Markus	Zeiningen	N/A	N/A	CH
Hostettler; Bernhard	Gockhausen	N/A	N/A	CH
Yang; Xiaogen	West Chester	OH	N/A	N/A

APPL-NO: 09/ 634067

DATE FILED: August 8, 2000

PARENT-CASE:

This is a Continuation Application of U.S. application Ser. No. 09/212,985, filed Dec. 16, 1998, which is incorporated herein by reference in its entirety. This application is also related to application Ser. No. 09/634,029, filed on even date herewith and entitled "Flavorant Compositions", and is incorporated herein by reference in its entirety.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
EP	97122633	December 22, 1997

US-CL-CURRENT: 560/130

ABSTRACT:

The invention is related to a flavorant composition containing 1'-acetoxychavicol acetate and 1'-acetoxyeugenol acetate derivatives thereof as well as a flavorant acceptable carrier. The flavorant composition may be used for flavoring foods, beverages or healthcare products with warm/hot, spicy and pungent sensations related to Galangal.

1 Claims, 0 Drawing figures

Exemplary Claim Number: 1

----- KWIC -----

Other Reference Publication - OREF (7):



Kondo, et al., 1'Acetoxychavicol **Acetate as a Potent Inhibitor of Tumor Promoter-induced** Epstein-Barr Virus Activation from Languas galanga, a Traditional Thai Condiment, Biosci, Biotech. Biochem. 57(8) (1993) 1344-1345.

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	6	glnap\$8	USPAT; US-PGPUB	2003/06/17 14:01
2	L2	331546	acetyl adj phosphate or acetylphosphate or acetate	USPAT; US-PGPUB	2003/06/17 14:02
3	L3	76345	promoter\$1	USPAT; US-PGPUB	2003/06/17 14:02
4	L4	1383639	induc\$8 or regulat\$8 or activat\$8 or modulat\$8	USPAT; US-PGPUB	2003/06/17 14:02
5	L5	60	2 near10 4 near10 3	USPAT; US-PGPUB	2003/06/17 14:03
6	L6	9302	pps or phosphoenol adj pyruvate adj synthase\$1	USPAT; US-PGPUB	2003/06/17 14:29
7	L7	94	6 near4 (gene\$1 or sequence\$1)	USPAT; US-PGPUB	2003/06/17 14:29
8	L8	22	7 same (overexpress\$ or amplif\$10 or increas\$8)	USPAT; US-PGPUB	2003/06/17 14:30

PGPUB-DOCUMENT-NUMBER: 20030059903

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030059903 A1

TITLE: Process for the production of L-amino acids using  
strains of the family enterobacteriaceae that contain an  
attenuated aceA gene

PUBLICATION-DATE: March 27, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Rieping, Mechthild	Bielefeld		DE	
Hermann, Thomas	Bielefeld		DE	

APPL-NO: 10/ 114048

DATE FILED: April 3, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60283384 20010413 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	101 16 518.8	2001DE-101 16 518.8	April 3, 2001

US-CL-CURRENT: 435/106, 435/252.3

ABSTRACT:

A process for the production of L-amino acids, in particular L-threonine, in which the following steps are carried out:

- (a) fermentation of the microorganisms of the family Enterobacteriaceae producing the desired L-amino acid, in which the aceA gene or nucleotide sequences coding therefor are attenuated, in particular are switched off,
- (b) enrichment of the L-amino acid in the medium or in the cells of the bacteria, and
- (c) isolation of the L-amino acid.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims priority to U.S. Provisional Application Serial No. 60/283,384, filed Apr. 13, 2001, the contents of which are incorporated herein by reference.

----- KWIC -----

Claims Text - CLTX (12):

11. The process of claim 1, wherein in the microorganism one or more of the genes selected from the following group is **overexpressed**: the thrABC operon coding for aspartate kinase, homoserine dehydrogenase, homoserine kinase and threonine synthase, the pyc **gene coding for pyruvate carboxylase, the pps gene coding for phosphoenol pyruvate synthase, the ppc gene** coding for phosphoenol pyruvate carboxylase, the pntA and pntB genes coding for transhydrogenase, the rhtB gene imparting homoserine resistance, the mqo gene coding for malate:quinone oxidoreductase, the rhtC gene imparting threonine resistance, and the thrE gene coding for threonine export.

PGPUB-DOCUMENT-NUMBER: 20030054503

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030054503 A1

TITLE: Process for the production of L-amino acids using  
strains of the family enterobacteriaceae that contain an  
attenuated dgsA gene

PUBLICATION-DATE: March 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Rieping, Mechthild	Bielefeld		DE	
Hermann, Thomas	Bielefeld		DE	

APPL-NO: 10/ 114043

DATE FILED: April 3, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60283384 20010413 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	101 16 518.8	2001DE-101 16 518.8	April 3, 2001

US-CL-CURRENT: 435/106, 435/252.33

ABSTRACT:

A process for the production of L-amino acids, in particular L-threonine, in which the following steps are carried out:

- (a) fermentation of the microorganisms of the family Enterobacteriaceae producing the desired L-amino acid, in which the dgsA gene or nucleotide sequences coding therefor are attenuated, in particular are switched off,
- (b) enrichment of the L-amino acid in the medium or in the cells of the bacteria, and
- (c) isolation of the L-amino acid.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims priority to U.S. Provisional Application Serial No. 60/283,384, filed Apr. 13, 2001, the contents of which are incorporated herein by reference.

----- KWIC -----

Claims Text - CLTX (12):

11. The process of claim 1, wherein in the microorganism one or more of the genes selected from the following group is **overexpressed**: the thrABC operon coding for aspartate kinase, homoserine dehydrogenase, homoserine kinase and threonine synthase, the pyc **gene coding for pyruvate carboxylase, the pps gene coding for phosphoenol pyruvate synthase, the ppc gene** coding for phosphoenol pyruvate carboxylase, the pntA and pntB genes coding for transhydrogenase, the rhtB gene imparting homoserine resistance, the mqo gene coding for malate:quinone oxidoreductase, the rhtC gene imparting threonine resistance, and the thrE gene coding for threonine export.

PGPUB-DOCUMENT-NUMBER: 20030049803

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030049803 A1

TITLE: Process for the production of L-amino acids using  
strains of the family enterobacteriaceae that contain an  
attenuated fruR gene

PUBLICATION-DATE: March 13, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Rieping, Mechthild	Bielefeld		DE	
Hermann, Thomas	Bielefeld		DE	

APPL-NO: 10/ 114073

DATE FILED: April 3, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60283384 20010413 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	101 16 518.8	2001DE-101 16 518.8	April 3, 2001

US-CL-CURRENT: 435/106, 435/252.3

ABSTRACT:

A process for the production of L-amino acids, in particular L-threonine, in which the following steps are carried out:

- (a) fermentation of the microorganisms of the family Enterobacteriaceae producing the desired L-amino acid, in which the fruR gene or nucleotide sequences coding therefor are attenuated, in particular are switched off, (
- b) enrichment of the L-amino acid in the medium or in the cells of the bacteria, and
- (c) isolation of the L-amino acid.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims priority to U.S. Provisional Application Serial No. 60/283,384, filed Apr. 13, 2001, the contents of which are incorporated herein by reference.

----- KWIC -----

Claims Text - CLTX (12):

11. The process of claim 1, wherein in the microorganism one or more of the genes selected from the following group is **overexpressed**: the thrABC operon coding for aspartate kinase, homoserine dehydrogenase, homoserine kinase and threonine synthase, the pyc **gene coding for pyruvate carboxylase, the pps gene coding for phosphoenol pyruvate synthase, the ppc gene** coding for phosphoenol pyruvate carboxylase, the pntA and pntB genes coding for transhydrogenase, the rhtB gene imparting homoserine resistance, the mqo gene coding for malate:quinone oxidoreductase, the rhtC gene imparting threonine resistance, and the thrE gene coding for threonine export.



PGPUB-DOCUMENT-NUMBER: 20030040103

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030040103 A1

TITLE: Fermentation process for the preparation of L-amino acids using strains of the family enterobacteriaceae

PUBLICATION-DATE: February 27, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Rieping, Mechthild	Bielefeld		DE	
Bastuck, Christine	Bielefeld		DE	
Hermann, Thomas	Bielefeld		DE	
Thierbach, Georg	Bielefeld		DE	

APPL-NO: 09/ 963668

DATE FILED: September 27, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60237610 20001004 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	DE 100 48 605.3	2000DE-DE 100 48 605.3	September 30, 2000
DE	DE 100 55 516.0	2000DE-DE 100 55 516.0	November 9, 2000
DE	DE 101 30 192.8	2001DE-DE 101 30 192.8	June 22, 2001

US-CL-CURRENT: 435/252.3

ABSTRACT:

The invention relates to a fermentation process for the preparation of L-amino acids, especially L-threonine, in which the following steps are carried out:

- fermentation of the microorganisms of the family Enterobacteriaceae producing the desired L-amino acid, in which microorganisms at least the pckA gene and/or the open reading frames yjfA and ytfP are, individually or jointly, attenuated and, in particular, switched off,
- enrichment of the L-amino acid in the medium or in the bacterial cells, and
- isolation of the L-amino acid.

----- KWIC -----

Claims Text - CLTX (7):

6. Process according to claim 1, wherein microorganisms of the family

Enterobacteriaceae in which one or more genes selected from the group comprising: 6.1 the thrABC operon coding for aspartate kinase, homoserine dehydrogenase, homoserine kinase and threonine synthase, 6.2 the pyc gene coding for pyruvate carboxylase, 6.3 the pps gene coding for phosphoenolpyruvate synthase, 6.4 the ppc gene coding for phosphoenolpyruvate carboxylase, 6.5 the pntA and pntB genes coding for transhydrogenase, 6.6 the rhtB gene for homoserine resistance, and 6.7 the rhtC gene for threonine resistance, 6.8 the gdhA gene coding for glutamate dehydrogenase are simultaneously amplified and, in particular, overexpressed are fermented for the preparation of L-amino acids.

PGPUB-DOCUMENT-NUMBER: 20030022218

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030022218 A1

TITLE: Gene targeting methods and vectors

PUBLICATION-DATE: January 30, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Burgess, Robert Marshall JR.	San Diego	CA	US	
Ji, Henry Hongjun	San Diego	CA	US	

APPL-NO: 10/ 185980

DATE FILED: June 26, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60300953 20010626 US

US-CL-CURRENT: 435/6, 435/320.1 , 800/13

ABSTRACT:

Methods and vectors are provided for the specific alteration of particular genetic loci in eukaryotic cells. One method includes the utilization of positive-positive selection (PPS) DNA vectors for the purpose of creating and identifying cells which have vector sequences integrated into the host cell genome via site-specific homologous recombination. The method also comprises the utilization of sequences encoding in vivo detectable markers for the identification of cells which have exogenous vector sequences integrated into the genome of the host cell, either via site-specific homologous recombination or nonhomologous recombination or insertion. The invention also includes vectors for creating modifications in eukaryotic cells.

RELATED APPLICATION DATA

[0001] The present application claims priority under 35 U.S.C. .sectn.119(e) to U.S. Provisional Application Serial No. 60/300,953 filed on Jun. 26, 2001, which is incorporated by reference herein.

----- KWIC -----

Detail Description Paragraph - DETX (38):

[0067] PPS vectors and methods as well as cotransformation methods are utilized for the purposes of creating and identifying cells which have

undergone site-specific homologous recombination between the vector and cellular endogenous genomic target sequences. The vectors substantially enrich for the identification of cells which have undergone said process. To "substantially enrich" refers to the ability to significantly increase the likelihood of identifying cells for which site-specific homologous recombination between the vector and cell DNA sequences. The significant increase in likelihood is at least two-fold of homologous recombination events when compared to nonspecific insertion or integration events, preferably at least 10-fold, more preferably at least 100-fold and even more preferably at least 10,000-fold. Substantially enriched cell populations derived from the use of PPS vectors include around 1%, more preferably 10%, and even more preferably 99% of cells isolated have undergone site-specific homologous recombination between PPS vector sequences and cellular endogenous genomic target sequences.

US-PAT-NO: 6573431

DOCUMENT-IDENTIFIER: US 6573431 B1

TITLE: Recombinant preduodenal lipases and polypeptides  
derivatives produced by plants, processes for obtaining  
them and their uses

DATE-ISSUED: June 3, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lenée; Philippe	Noumea	N/A	N/A	FR
Gruber; Veronique	Chamalieres	N/A	N/A	FR
Baudino; Sylvie	Orcines	N/A	N/A	FR
Merot; Bertrand	Volvic	N/A	N/A	FR
Benicourt; Claude	Houilles	N/A	N/A	FR
Cudrey; Claire	Gieres	N/A	N/A	FR

APPL-NO: 09/ 348930

DATE FILED: July 2, 1999

PARENT-CASE:

The present invention is a continuation of U.S. Ser. No. 08/945,321, filed Feb. 12, 1998, now abandoned, which was the national stage of PCT/FR96/00606, filed Apr. 19, 1996, which claims priority to FR9504754, filed Mar. 20, 1995.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
FR	95/04754	April 20, 1995

US-CL-CURRENT: 800/295, 435/320.1, 435/410, 435/411, 435/412, 435/414,  
435/415, 435/416, 435/417, 536/23.1, 536/23.5, 800/278,  
800/288, 800/298, 800/305, 800/306, 800/312, 800/317,  
800/317.2, 800/317.3, 800/317.4, 800/320, 800/320.1,  
800/320.2, 800/320.3, 800/322

ABSTRACT:

The invention concerns the use of recombinant nucleotides sequences containing cDNA coding for a preduodenal lipase, or any sequence derived from this cDNA, for transforming plant cells in order to obtain recombinant preduodenal lipase or polypeptide derivatives.

The invention also concerns the use of genetically modified plants or parts thereof, or extracts of these plants or the use of recombinant preduodenal lipase or resultant polypeptide derivatives in the field of foodstuffs, or for producing medicaments, or in industry.

11 Claims, 8 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 8

----- KWIC -----

Detailed Description Text - DETX (135):

The plasmid pBIOC22 was digested totally by BglII and partly by HindIII in order to suppress the sequence which codes for the polypeptide Leu-Phe-Gly-Lys (first 4 amino acids) of the mature DGL protein. This sequence was replaced by that which codes for the signal peptide PS of 23 amino acids (ATG AAA GCC TTC ACA CTC GCT CTC TTC TTA GCT CTT TCC CTC TAT CTC CTG CCC AAT CCA GCC CAT TCC AGG TTC AAT CCC ATC CGC CTC CCC ACC ACA CAC GAA CCC GCC) (SEQ ID NO: 17) fused to that of the first 4 codons of the sequence which codes for the mature DGL protein ("PPS-first 4 codons of mature DGL"). The sequence "PPS-first 4 codons for mature DGL" was amplified by PCR using the plasmid pMAT103 (Matsuoka and Nakamura, 1991) with the aid of the 2 following oligodeoxynucleotides 5' caggagatctgATG AAA GCC TTC ACA CTC GC 3'(SEQ ID NO: 15) and 5' ATG AAG CTT TCC AAA CAA GGA GGG TTC GTG TGT GGT TG 3' (SEQ ID NO: 18), in accordance with the protocol of PCR amplification described above in paragraph I. After double enzymatic digestion by BglII and HindIII, the DNA fragments originating from the PCR amplification were purified by electrophoresis over 2% agarose gel, electroeluted (Sambrook et al., 1989), precipitated in the presence of 1/10 volume of 3M sodium acetate, pH 4.8, and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 min, centrifuged at 12,000 g for 30 min, washed with 70% ethanol, dried and then ligated to the plasmid DNA of pBIOC22, which had been doubly digested by BglII and HindIII, purified by electrophoresis over 0.8% agarose gel, electroeluted, subjected to precipitation with alcohol, dried and dephosphorylated by the alkaline phosphatase enzyme of the intestine of the calf (Boehringer Mannheim) in accordance with the manufacturer's instructions. The ligation was carried out with 100 ng of the dephosphorylated vector described above and 50 ng of the digested DNA fragments, originating from the PCR amplification, described above in a reaction medium of 10 .mu.l in the presence of 1 .mu.l of the buffer T4 DNA ligase.times.10 (Amersham) and 2.5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria Escherichia coli Dh5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 50 .mu.g/ml of ampicillin, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes.

US-PAT-NO: 6489100

DOCUMENT-IDENTIFIER: US 6489100 B1

TITLE: Microorganisms and methods for overproduction of DAHP by  
cloned PPS gene

DATE-ISSUED: December 3, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Liao; James C.	Los Angeles	CA	N/A	N/A

APPL-NO: 09/ 440503

DATE FILED: November 15, 1999

PARENT-CASE:

This is a request for filing a Continuation under 37 C.F.R. .sctn.1.60 of prior Ser. No. 08/801,454 filed on Feb. 18, 1997, now U.S. Pat. No. 5,906,925, and of prior Ser. No. 09/277,183 filed on Mar. 26, 1999, to be issued as U.S. Pat. No. 5,985,617, both of JAMES C. LIAO for MICROORGANISMS AND METHODS FOR OVERPRODUCTION OF DAHP BY CLONED PPS GENE.

US-CL-CURRENT: 435/6, 435/105, 435/108, 435/200, 435/72, 536/23.2  
, 536/23.7, 536/24.1

ABSTRACT:

Genetic elements comprising expression vectors and a gene coding for phosphoenol pyruvate synthase is utilized to enhance diversion of carbon resources into the common aromatic pathway and pathways branching therefrom. The overexpression of phosphoenol pyruvate synthase increases DAHP production to near theoretical yields.

10 Claims, 14 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 6

----- KWIC -----

Abstract Text - ABTX (1):

Genetic elements comprising expression vectors and a gene coding for phosphoenol pyruvate synthase is utilized to enhance diversion of carbon resources into the common aromatic pathway and pathways branching therefrom.

The overexpression of phosphoenol pyruvate synthase increases DAHP production to near theoretical yields.

Brief Summary Text - BSTX (18):

The present invention provides genetically engineered strains of microorganisms that overexpress the pps gene for increasing the production of DAHP to near theoretical yields. The present invention also provides genetically engineered strains of microorganisms where at least one of the plasmids pPS341, pPSL706, pPS706, or derivatives thereof is transformed into a microorganism for increasing the production of DAHP to near theoretical yields.

Brief Summary Text - BSTX (19):

The present invention further provides a method for increasing carbon flow for the biosynthesis of DAHP in a host cell comprising the steps of transforming into the host cell recombinant DNA comprising a pps gene so that Pps is expressed at enhanced levels relative to wild type host cells, concentrating the transformed cells through centrifugation, resuspending the cells in a minimal, nutrient lean medium, fermenting the resuspended cells, and isolating DAHP from the medium.

Brief Summary Text - BSTX (20):

The present invention further provides methods of increasing carbon flow into the common aromatic pathway of a host cell comprising the step of transforming the host cell with recombinant DNA comprising a pps gene so that Pps is expressed at appropriate point in the metabolic pathways at enhanced levels relative to wild type host cells.

Detailed Description Text - DETX (3):

The inventor have found that cell lines can be developed that increase the carbon flux into DAHP production and achieve near theoretical yields of DAHP by overexpressing phosphoenolpyruvate synthase (Pps) in the cell lines. Overexpression of Pps can increase the final concentration and yield of DAHP by as much as two-fold, to a near theoretical maximum as compared to wild type cell lines. The overexpression of Pps is achieved by transforming a cell line with recombinant DNA comprising a pps gene so that Pps is expressed at enhanced level relative to the wild type cell line and so that the yield of DAHP approaches its theoretical value.

Detailed Description Text - DETX (5):

Besides the use of the pps gene, the present invention also provides for transfer of genetic elements comprising the tkt gene, the gene coding for DAHP synthase (aroF in E. coli), the gene coding for 3-dehydroquinate synthase (aroB in E. coli), or other genes encoding enzymes that catalyze reactions in the common aromatic pathway. Such a cell transformation can be achieved by transferring one or more plasmids that contain genes that code for enzymes that increase the carbon flux for DAHP synthesis and for subsequent synthesis of other desired cyclic, pre-aromatic, and aromatic metabolites. As a result of



this transfer of genetic element(s), more carbon enters and moves through the common aromatic pathway relative to wild type host cells not containing the genetic elements of the present invention.

Detailed Description Text - DETX (6):

In one embodiment, the present invention comprises a method for **increasing** carbon flow into the common aromatic pathway of a host cell by **increasing** the production of DAHP through the **overexpression** of Pps at the appropriate point in the common aromatic pathway to provide additional PEP at the point where PEP condenses with E4P. **Increasing** carbon flow requires the step of transforming the host cell with recombinant DNA containing a **pps gene so that Pps is overexpressed** at enhanced levels relative to wild type host cells. DAHP is then produced by fermentation of the transformed cell in a nutrient medium where the DAHP can be extracted from the medium on a batch wise or continuous extraction procedure.

Detailed Description Text - DETX (7):

In another embodiment, the present invention involves the co-**overexpression of a pps gene** and other genes coding for enzymes of the common aromatic pathway where additional genetic material is transformed into the host cell. The genes transferred can include the tkt gene, DAHP synthase gene and DHQ synthase gene (preferably the aroF or aroB genes, respectively). Although the work so far has centered around transforming certain host cell strains of E. coli such as AB2847 aroB, this particular host cell may not be the preferred host cells for the commercial production of DAHP or DAHP metabolites through the **overexpression** of Pps.

Detailed Description Text - DETX (8):

Another embodiment of the present invention is a method for enhancing a host cell's biosynthetic production of compounds derived from the common aromatic pathway. This method involves the step of **increasing** expression of Pps in the host cell relative to a wild type host cell. The step of **increasing** expression of Pps can include transferring into the host cell a vector carrying the **pps gene**. The **overexpression** of Pps results in forcing **increased** carbon flow into the biosynthesis of DAHP.

Detailed Description Text - DETX (9):

In another embodiment of the present invention, a method for enhancing a host cell's biosynthetic production of compounds derived from the common aromatic pathway relative to wild type host cell's biosynthetic production of such compound is provided. This method requires the step of **increasing** expression in a host cell of a protein catalyzing conversion of pyruvate to PEP. The expression of such a protein can involve transferring into the host cell recombinant DNA including a **pps gene**.

Detailed Description Text - DETX (55):

One preferred embodiment of the present invention encompasses modification

of a host cell to cause overexpression of an enzyme having the catalytic properties of naturally derived Pps, and, thereby maximizing the yield of DAHP to near theoretical yields. Enzymes having the catalytic activity of Pps include, but are not limited to, Pps produced by expression in whole cells of a naturally derived pps gene, enzymes produced by expression in whole cells of a naturally derived pps gene modified by sequence deletion or addition so that the expressed enzyme has an amino acid sequence that varies from unmodified Pps, abzymes produced to have catalytic sites with steric and electronic properties corresponding to catalytic sites of Pps, or other proteins produced to have the capability of catalyzing the conversion of pyruvate to PEP by any other art recognized means.

Detailed Description Text - DETX (57):

Additionally, the transformation of DNA, including the pps gene, into microorganisms engineered for the overexpression of other substrates, and/or overexpression or derepression of enzymes in the pentose phosphate or common aromatic pathway can be used to tailor the microorganism to achieve near theoretical yields of such DAHP metabolites as tyrosine, tryptophan, phenylalanine, and other aromatic metabolites such as indigo, catechol and quinoid organics such as quinic acid, benzoquinone, and hydroquinone.

Detailed Description Text - DETX (91):

This example demonstrates that the E. Coli AB2847 is unable to utilize DAHP, and accumulates DAHP in the medium if DAHP synthase is overexpressed. This strain was used as a host for detecting the flux committed to the aromatic pathways. Since Draths et al. (Draths, K. M., D. L. Pompliano, D. L. Conley, J. W. Frost, A. Berry, G. L. Disbrow, R. J. Staversky, and J. C. Lievense, "Biocatalytic synthesis of aromatics from D-glucose: The role of transketolase," J. Am. Chem. Soc., 1992, 114, 3956-3962) have shown a possible limitation in the production of DAHP by E4P, pAT1 (containing both aroG.sup.fbr and tktA) was transformed into AB2847 to eliminate the limitation of E4P. To test whether PEP supply limits DAHP production, PEP synthase (Pps) was overexpressed in AB2847/pAT1 by transforming plasmid pPS341 into this strain. 20-70 copies of the pps gene were expressed in the host cells. As a control, pPS341 was substituted by pPS341.times.1, which encodes an inactive, but stable pps gene product. The use of the inactive Pps control allowed discrimination between the effect of Pps activity and that of protein overexpression.

Detailed Description Text - DETX (97):

As shown above, Pps overexpression improved DAHP production from glucose. We were interested to know whether the basal level of Pps expression in glucose medium contributed to the production of DAHP. Therefore, the chromosomal pps gene in strain AB2847 was knocked out. The resulting strain (JCL1362) was used as the host to repeat the above experiments. Results show that inactivation of chromosomal pps did not significantly affect the DAHP production in strains containing pRW5 or pAT1 (FIG. 2B). Therefore, the basal level of pps expression in glucose medium did not contribute to the DAHP production.

Detailed Description Text - DETX (116):

Quinoid organics can be derived from dehydroquinone which is a down-stream metabolite of DAHP. To produce quinic acid, *E. coli* AB2848 *aroD* harboring pTW8090A which contains the gene *qad* (quinic acid dehydrogenase from *Klebsiella pneumoniae*) (ref: Draths, Ward, and Frost, 1992, JACS, 114, 9725-9726), and pKD136 (ref: same as above) which contains *tkt*, *aroF*, and *aroB* genes can be used as a host. The **pps gene** can be cloned into one of these plasmids and be simultaneously **overexpressed**. It has been reported that at least 80 mM of D-glucose can be converted into 25 mM of quinic acid. After cell removal, quinic acid in the supernatant can be converted into benzoquinone after addition of sulfuric acid and technical grade manganese (IV) dioxide and heating at 100.degree. C. for 1 h. In the absence of acidification, aqueous solutions of purified quinic acid were converted to hydroquinone in 10% yield upon heating at 100.degree. C. for 18 h with technical grade manganese dioxide.

Claims Text - CLTX (7):

7. A process for the production of DAHP which comprises cultivating a microorganism in a nutrient medium and **overexpressing the Pps gene**.

Claims Text - CLTX (8):

8. The process of claim 7 wherein the step of **overexpressing the Pps gene** comprises transforming a plasmid selected from the group consisting of pPS341, pPSL706, and pPS706 into the microorganism.

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	6	glnap\$8	USPAT; US-PGPUB	2003/06/17 14:01
2	L2	331546	acetyl adj phosphate or acetylphosphate or acetate	USPAT; US-PGPUB	2003/06/17 14:02
3	L3	76345	promoter\$1	USPAT; US-PGPUB	2003/06/17 14:02
4	L4	1383639	induc\$8 or regulat\$8 or activat\$8 or modulat\$8	USPAT; US-PGPUB	2003/06/17 14:02
5	L5	60	2 near10 4 near10 3	USPAT; US-PGPUB	2003/06/17 14:03
6	L6	9302	pps or phosphoenol adj pyruvate adj synthase\$1	USPAT; US-PGPUB	2003/06/17 14:29
7	L7	94	6 near4 (gene\$1 or sequence\$1)	USPAT; US-PGPUB	2003/06/17 14:29
8	L8	22	7 same (overexpress\$ or amplif\$10 or increas\$8)	USPAT; US-PGPUB	2003/06/17 14:30
9	L9	17	7 and 2	USPAT; US-PGPUB	2003/06/17 14:48

PGPUB-DOCUMENT-NUMBER: 20030003573

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030003573 A1

TITLE: Hepatocytes for therapy and drug screening made from  
embryonic stem cells

PUBLICATION-DATE: January 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Rambhatle, Lakshmi	Redwood City	CA	US	
Carpenter, Melissa K.	Castro Valley	CA	US	

APPL-NO: 10/ 087142

DATE FILED: March 1, 2002

RELATED-US-APPL-DATA:

child 10087142 A1 20020301

parent continuation-in-part-of 10001267 20011031 US PENDING

child 10001267 20011031 US

parent continuation-in-part-of 09872182 20010531 US PENDING

non-provisional-of-provisional 60200095 20000427 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
US	PCT/US01/13471	2001US-PCT/US01/13471	April 26, 2001
WO	01/81549	2000WO-01/81549	November 1, 2000

US-CL-CURRENT: 435/366, 435/370

ABSTRACT:

It has been discovered that when pluripotent stem cells are cultured in the presence of a hepatocyte differentiation agent, a population of cells is derived that has a remarkably high proportion of cells with phenotypic characteristics of liver cells. In one example, human embryonic stem cells are allowed to form embryoid bodies, and then combined with the differentiation agent n-butyrate, optionally supplemented with maturation factors. In another example, n-butyrate is added to human embryonic stem cells in feeder-free culture. Either way, a remarkably uniform cell population is obtained, which is predominated by cells with morphological features of hepatocytes, expressing surface markers characteristic of hepatocytes, and having enzymatic and

biosynthetic activity important for liver function. Since stem cells readily proliferate in culture, this system provides an abundant source of cells of the hepatocyte lineage for a variety of applications, such as drug screening, and replenishing liver function in the context of clinical treatment.

#### REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation-in-part of pending U.S. utility application 10/001,267, filed Oct. 31, 2001, which is a continuation-in-part of U.S. Ser. No. 09/872,182, filed May 31, 2001; and International Patent Application PCT/US01/13471, filed Apr. 26, 2001 (designating the U.S. and published as WO 01/81549 on Nov. 1, 2001); which in turn claims priority to U.S. provisional patent application No. 60/200,095, filed Apr. 27, 2000.

[0002] This application claims the priority benefit of all the aforelisted applications. The four priority documents are hereby incorporated herein by reference in their entirety, along with U.S. utility application 09/718,308, and International Patent Publication WO 01/51616.

----- KWIC -----

#### Detail Description Paragraph - DETX (107):

[0132] Matched hepatocyte lineage cells with allotypic differences can be obtained in the following fashion. pPS cells in feeder-free culture are genetically modified according to the techniques described in International Patent Publication WO 01/51616 (Geron Corp.). Modifications are made to a particular p450 component or other drug metabolizing enzyme to alter its function in a manner that makes it resemble a less frequent but naturally occurring allotype. For example, where the naturally occurring variant results in loss of expression or expression of a non-functional protein, then the corresponding gene in pPS cells can simply be modified to remove transcription or translation start signals. Where the natural allotype causes expression of mutant enzyme, then the corresponding gene in pPS cells can be replaced with the mutant form (either by replacing the endogenous gene, or inserting the mutant transgene elsewhere). Homologous recombination using an appropriate targeting vector can achieve any of these changes, but any suitable genetic manipulation technique can be used. The modification can be made in a heterozygous or homozygous fashion.

#### Detail Description Paragraph - DETX (164):

[0187] RT-PCR analysis of expression at the transcription level was conducted as follows: RNA was extracted from the cells using RNAeasy Kit.TM. (Qiagen) as per manufacturer's instructions. The final product was then digested with DNase to get rid of contaminating genomic DNA. The RNA was incubated in RNA guard (Pharmacia Upjohn) and DNase I (Pharmacia Upjohn) in buffer containing 10 mM Tris pH 7.5, 10 mM MgCl.sub.2, and 5 mM DDT at 37.degree. C. for 30-45 minutes. To remove protein from the sample, phenol chloroform extraction was performed and the RNA precipitated with 3 M sodium acetate and 100% cold ethanol. The RNA was washed with 70% ethanol, and the pellet was air-dried and resuspended in DEPC-treated water. For the reverse

transcriptase (RT) reaction, 500 ng of total RNA was combined with a final concentration of 1.times. First Strand Buffer (Gibco), 20 mM DDT and 25 .mu.g/mL random hexamers (Pharmacia Upjohn). The RNA was denatured for 10 min at 70.degree. C., followed by annealing at room temperature for 10 min. dNTPs were added at a final concentration of 1 mM along with 0.5 .mu.L of Superscript II RT (Gibco), incubated at 42.degree. C. for 50 minutes, and then heat-inactivated at 80.degree. C. for 10 min. Samples were then stored at -20.degree. C. till they were processed for PCR analysis. Standard polymerase chain reaction (PCR) was performed using primers specific for the markers of interest in the following reaction mixture: cDNA 1.0 .mu.L, 10.times.PCR buffer (Gibco) 2.5 .mu.L, 10.times.MgCl.sub.2 2.5 .mu.L, 2.5 mM dNTP 3.0 .mu.L, 5 .mu.M 3'-primer 1.0 .mu.L, 5 .mu.M 5'-primer, 1.0 .mu.L, Taq 0.4 .mu.L, DEPC-water 13.6 .mu.L. Selected markers and reaction conditions are shown in Table 3.

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TITLE: Method for producing hemin proteins using plant cells,  
resulting proteins and products containing same

PUBLICATION-DATE: December 19, 2002

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FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
FR	95/08615	1995FR-95/08615	July 17, 1995

US-CL-CURRENT: 800/288, 800/282

ABSTRACT:

A method for producing haemin proteins by (i) inserting into plant cells one or more nucleic acid molecules that each comprise at least one sequence coding for a protein component of an animal haemin protein capable of reversibly binding oxygen, or for a variant or portion of said protein component, and optionally a sequence coding for a selection agent; (ii) selecting cells containing nucleic



acid coding for the protein component of the haemin protein; (iii) optionally propagating the transformed cells either in a culture or by regenerating whole transgenic or chimeric plants; and (iv) recovering and optionally purifying a haemin protein that includes a complex consisting of the protein or proteins coded for by said nucleic acid and at least one iron-containing porphyrinic nucleus, or a plurality of such complexes.

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Detail Description Paragraph - DETX (10):

[0130] The plasmid DNA of the clones obtained, selected on 12 .mu.g/ml tetracycline, was extracted according to the alkaline lysis method (Birnboim and Doly, 1979) and analyzed by enzymatic digestion with restriction enzymes. Next, the HindIII restriction site of the plasmid DNA of the selected clone was modified at an EcoRI restriction site with the aid of a phosphorylated HindIII-EcoRI adaptor (Stratagene Cloning Systems). To carry out this modification, 500 ng of plasmid DNA of the selected clone were digested with HindIII, dephosphorylated with the enzyme calf intestinal alkaline phosphatase (Boeringer Mannheim) according to the manufacturer's recommendations and coprecipitated in the presence of 1500 ng of HindIII-EcoRI adaptor DNA, 1/10 volume of 3 M sodium acetate pH 4.8 and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 min. After centrifugation at 12000 g for 30 min, the precipitated DNA was washed with 70% ethanol, dried, taken up in 8 .mu.l of water, heated at 65.degree. C. for 10 min, and then ligated in the presence of 1 .mu.l of 10.times. T4 DNA ligase buffer (Amersham) and 2.5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. After inactivation of the T4 DNA ligase at 65.degree. C. for 10 min, the ligation reaction mixture was digested with EcoRI, purified by electrophoresis on a 0.8% agarose gel, electroeluted (Sambrook et al., 1989), precipitated in the presence of 1/10 volume of 3 M sodium acetate pH 4.8 and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 min, centrifuged at 12000 g for 30 min, washed with 70% ethanol and then dried. The E. coli DH5.alpha. bacteria previously made competent were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 12 .mu.g/ml tetracycline was extracted according to the alkaline lysis method (Birnboim and Doly, 1979) and analyzed by enzymatic digestion with HindIII and EcoRI in particular. The resulting binary plasmid, which now possesses only the last 9 codons of the coding sequences of the cat gene and in which the EcoRI site is unique, was called pBIOC4.

Detail Description Paragraph - DETX (12):

[0132] The expression cassette, consisting of the pd35S promoter and the 35S polyA terminator, was isolated from the plasmid pJIT163D. The plasmid pJIT163D is derived from the plasmid pJIT163 which is itself derived from the plasmid pJIT60 (Guerineau and Mullineaux, 1993). The plasmid pJIT163 possesses an ATG codon between the HindIII and Sall sites of the polylinker. To eliminate this ATG and to obtain the plasmid pJIT163D, the plasmid DNA pJIT163 was doubly digested with HindIII and Sall, purified by electrophoresis on a 0.8% agarose gel, electroeluted (Sambrook et al., 1989), precipitated in the presence of 1/10 volume of 3 M sodium acetate pH 4.8 and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 min, centrifuged at 12000 g for 30 min, washed with 70%

ethanol, dried, subjected to the action of the Klenow enzyme (New England Biolabs) according to the manufacturer's recommendations, deproteinized by extraction with 1 volume of phenol:chloroform:isoamyl alcohol (25:24:1) and then 1 volume of chloroform:isoamyl alcohol (24:1), precipitated in the presence of 1/10 volume of 3 M sodium acetate pH 4.8 and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 min, centrifuged at 12000 g for 30 min, washed with 70% ethanol, dried and finally ligated in the presence of 1 .mu.l of 10.times. T4 DNA ligase buffer (Amersham) and 2.5 U of T4 DNA ligase enzyme (Amersham) at 14.degree. C. for 16 hours. The E. coli DH5a bacteria previously made competent, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 50 .mu.g/ml ampicillin, was extracted according to the alkaline lysis method (Birnboim and Doly, 1979) and analyzed by enzymatic digestion with restriction enzymes. To isolate the expression cassette consisting of the pd35S promoter and of the 35S polyA terminator (Sacl-XhoI fragment), the plasmid DNA of the pJIT163D clone selected was digested with SacI and XhoI. The SacI-XhoI-fragment, carrying the expression cassette, was purified by electrophoresis on a 0.8% agarose gel, electroeluted (Sambrook et al., 1989) precipitated in the presence of 1/10 volume of 3 M sodium acetate pH 4.8 and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 min, centrifuged at 12000 g for 30 min, washed with 70% ethanol, dried and then subjected to the action of Mung Bean nuclease enzyme (New England Biolabs) according to the manufacturer's recommendations. This purified insert (200 ng) was cloned into the plasmid DNA of pBIOC4 (20 ng) digested with EcoRI, treated with the Mung Bean nuclease enzyme and dephosphorylated with the enzyme calf intestinal alkaline phosphatase (Boehringer Mannheim) according to the manufacturer's recommendations. The ligation reaction was carried out in 20 .mu.l, in the presence of 2 .mu.l of 10.times. T4 DNA ligase buffer (Amersham), 2 .mu.l of 50% polyethylene glycol 8000 and 5 U of T4 DNA ligase enzyme (Amersham) at 14.degree. C. for 16 hours. The E. coli DH5.degree. C. bacteria previously made competent were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 12 .mu.g/ml tetracyclin was extracted according to the alkaline lysis method (Birnboim and Doly, 1979) and analyzed by enzymatic digestion with restriction enzymes. The resulting plasmid was called pBIOC21.

Detail Description Paragraph - DETX (15):

[0135] The co-expression binary plasmid is derived from pBIOC21. It contains two expression cassettes each consisting of a pd35S promoter and a 35S polyA terminator but differ in the polylinker separating the promoter from the terminator. One of the expression cassettes is that of pBIOC21 already described in paragraph I.a. The other expression cassette was obtained by replacing the HindIII-BamHI-SmaI-EcoRI polylinker of pJIT163D (described in paragraph I.a.) by a HindIII-EcoRI adaptor carrying the PaeI, Ascl, MluI and HpaI restriction sites. This adaptor was obtained by renaturation of the 2 oligodeoxynucleotides WD11 (5' AGC TGA TTA ATT AAG GCG CGC CAC GCG TTA AC 3') and WD12 (5' AAT TGT TAA CGC GTG GCG CGC CTT AAT TAA TC 3') which are complementary for their 28 terminal 3' nucleotides. One hundred .mu.M of each of these two oligodeoxynucleotides were previously phosphorylated by the action of 10 U of T4 polynucleotide kinase enzyme (New England Biolabs) in a total reaction volume of 10 .mu.l containing 1 .mu.l of 10.times. T4 polynucleotide kinase buffer (New England Biolabs) and 3 .mu.l of ATP (95 mM). The two reaction mixtures were incubated at 37.degree. C. for 1 hour, and then at

65.degree. C. for 20 min. They were then combined and their volume was adjusted to 500 .mu.l. After extraction with 1 volume of phenol:chloroform:isoamyl alcohol (25:24:1) and 1 volume of chloroform:isoamyl alcohol (24:1), 50 .mu.l of 3 M sodium acetate pH 6.0 were added. The reaction mixture was incubated at 80.degree. C. for 10 min and then cooled slowly to room temperature. The DNA was then precipitated in the presence of 2.5 volumes of absolute ethanol at -80.degree. C. for 30 min, centrifuged at 14000 g at 4.degree. C. for 1 hour, washed with 70% ethanol, centrifuged at 14000 g at 4.degree. C. for 10 min, dried, taken up in 10 .mu.l of H<sub>2</sub>O. The HindIII-EcoRI DNA fragment was then cloned at the HindIII-EcoRI sites of the plasmid DNA pJIT163D previously dephosphorylated with the enzyme calf intestinal alkaline phosphatase (New England Biolabs) according to the manufacturer's recommendations. The ligation reaction was carried out in a reaction volume of 20 .mu.l in the presence of 1 U of T4 DNA ligase (Gibco-BRL) for a total DNA concentration of 8.5 nM with a vector/insert molar ratio of 1 and of 4 .mu.l of 5.times. T4 DNA ligase buffer (Gibco-BRL) at 25.degree. C. for 16 hours. The E. coli DH5.alpha. bacteria previously made competent were transformed (Hanahan, 1985). The plasmid DNA of the clones obtained, selected on 100 .mu.g/ml ampicillin, was extracted according to the alkaline lysis method (Stephen et al., 1990) and analyzed by enzymatic digestion. The resulting clone was called pBIOC42. Its validity was verified by sequencing with the aid of the "Sequenase Version 2.0 DNA Sequencing" kit marketed by United States Biochemical (USB) according to the dideoxynucleotides method (Sanger et al., 1977). The reaction conditions follow the manufacturer's recommendations except for the denaturation and hybridization. The reaction medium containing the plasmid DNA (0.5 to 1 pmol), the oligonucleotide primer (2 pmol), 10% DMSO and the 1x reaction buffer (USB), is incubated at 100.degree. C. for 10 min, then suddenly cooled to -80.degree. C. in dry ice.

Detail Description Paragraph - DETX (26):

[0146] The third stage was the PCR amplification of the complete cDNA encoding the .alpha. globin chain (142 codons including the initiator ATG). The two types of DNA fragments amplified in the first and second stages served as template DNA and the two primers used were WD13 and WD14. The PCR amplification was carried out as described in the first stage except that the hybridization temperature of the cycle is 60.degree. C. The amplified DNA fragments were then extracted with H.sub.2O-saturated ether after having adjusted the volume to 500 .mu.l with TE buffer (10 mM Tris-HCl pH 8.0, 1 mM EDTA). After extraction with 1 volume of phenol:chloroform:isoamyl alcohol (25:24: 1) and 1 volume of chloroform:isoamyl alcohol (24: 1), the DNA fragments were precipitated in the presence of 1/10 volume of 3 M sodium acetate pH 6.0 and 2 volumes of absolute ethanol at -80.degree. C. for 30 min, centrifuged at 14000 g at 4.degree. C. for 30 min, washed with 70% ethanol, centrifuged at 14000 g at 4.degree. C. for 10 min, dried, taken up in 50 .mu.l of H.sub.2O. Next, 25 .mu.l of these DNA fragments were doubly digested with HindIII and EcoRI, purified by electrophoresis on 1.8% agarose gel and by the action of the "Geneclean 11" kit (BIO101) and cloned at the HindIII and EcoRI sites of the plasmid pNEB193 marketed by New England Biolabs, and previously dephosphorylated with the enzyme calf intestinal alkaline phosphatase (New England Biolabs) according to the manufacturer's recommendations. The ligation and the transformation were carried out as described in section I.b. The plasmid DNA of the clones obtained, selected on 100 .mu.g/ml ampicillin, was

extracted according to the alkaline lysis method (Stephen et al., 1990) and analyzed by enzymatic digestion. The resulting clone was called pBIOC44. The nucleotide sequence of the cDNA encoding the recombinant .alpha. globin chain was verified by sequencing with the aid of the "Sequenase Version 2.0 DNA Sequencing" kit marketed by United States Biochemical (USB) as described in section I.b. The sequencing revealed two silent mutations situated at the forty-eighth nucleotide (C modified to T) and at the fifty-fourth (T modified to C) of the coding sequence for the .alpha. globin chain.

Detail Description Paragraph - DETX (99):

[0219] To allow vacuolar targeting, the sequence encoding the prepropeptide (PPS) of sporamine A of the tuberized roots of sweet potato (Murakami et al., 1986; Matsuoka and Nakamura, 1991), which corresponds to the signal peptide followed by the N-terminal sequence for vacuolar targeting (ATG AAA GCC TTC ACA CTC GCT CTC TTC TTA GCT CTT TCC CTC TAT CTC CTG CCC AAT CCA GCC CAT TCC AGG TTC AAT CCC ATC CGC CTC CCC ACC ACA CAC GAA CCC GCC), is fused with the first codon of the sequence encoding, on the one hand, the mature .alpha. globin chain (deletion of the initiator ATG) and, on the other hand, the mature .beta. globin chain (deletion of the initiator ATG) while maintaining the open reading frames. This prepropeptide of 37 amino acids was isolated from the plasmid pMAT103 (Matsuoka and Nakamura, 1991) and used during the carrying out of the constructions.

US-PAT-NO: 6573431

DOCUMENT-IDENTIFIER: US 6573431 B1

TITLE: Recombinant preduodenal lipases and polypeptides  
derivatives produced by plants, processes for obtaining  
them and their uses

DATE-ISSUED: June 3, 2003

INVENTOR-INFORMATION:

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APPL-NO: 09/ 348930

DATE FILED: July 2, 1999

PARENT-CASE:

The present invention is a continuation of U.S. Ser. No. 08/945,321, filed Feb. 12, 1998, now abandoned, which was the national stage of PCT/FR96/00606, filed Apr. 19, 1996, which claims priority to FR9504754, filed Mar. 20, 1995.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
FR	95/04754	April 20, 1995

US-CL-CURRENT: 800/295, 435/320.1, 435/410, 435/411, 435/412, 435/414,  
435/415, 435/416, 435/417, 536/23.1, 536/23.5, 800/278,  
800/288, 800/298, 800/305, 800/306, 800/312, 800/317,  
800/317.2, 800/317.3, 800/317.4, 800/320, 800/320.1,  
800/320.2, 800/320.3, 800/322

ABSTRACT:

The invention concerns the use of recombinant nucleotides sequences containing cDNA coding for a preduodenal lipase, or any sequence derived from this cDNA, for transforming plant cells in order to obtain recombinant preduodenal lipase or polypeptide derivatives.

The invention also concerns the use of genetically modified plants or parts thereof, or extracts of these plants or the use of recombinant preduodenal lipase or resultant polypeptide derivatives in the field of foodstuffs, or for producing medicaments, or in industry.

11 Claims, 8 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 8

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Detailed Description Text - DETX (44):

The invention more particularly relates to a process for the preparation of the abovementioned recombinant DGL and/or polypeptide (.DELTA.54) and/or polypeptide (.DELTA.4), characterized in that it comprises: transformation of explant cells of a plant (in particular explants of leaves) by bringing the latter together with a strain of *Agrobacterium tumefaciens* transformed by a plasmid as described above containing the recombinant nucleotide sequence pd35S-PS-DGL and/or the sequence pd35S-PPS-DGL, selection of the transformed explants on a medium containing kanamycin, production of transformed plants from the abovementioned transformed explants by culture of the latter on suitable media, extraction of the recombinant DGL and/or the polypeptide (.DELTA.54) and/or the polypeptide (.DELTA.4), in particular by grinding the leaves and/or the seeds and/or the fruits of the abovementioned transformed plants in a suitable buffer, centrifugation and recovery of the supernatant constituting the plant extract of enzymatic activity, where appropriate, purification of the recombinant DGL and/or the polypeptide (.DELTA.54) and/or the polypeptide (.DELTA.4) from the extract obtained during the preceding stage, in particular by chromatography carried out on the supernatant, which leads to the preparation of the recombinant DGL and/or the polypeptide (.DELTA.54) and/or the polypeptide (.DELTA.4) in an essentially pure form.

Detailed Description Text - DETX (47):

The invention more particularly relates to a process for the preparation of recombinant DGL and/or the polypeptide (.DELTA.54) and/or the polypeptide (.DELTA.4), characterized in that it comprises: transformation of explant cells of a plant by bringing the latter together with a strain of *Agrobacterium tumefaciens* transformed by a plasmid as described above containing the recombinant nucleotide sequence pCRU-PPS-DGL and/or the sequence pCRU-PS-DGL and/or the sequence pGEA1-RGLSP-DGL and/or the sequence pGEA6-RGLSP-DGL and/or the sequence pAR-IAR-RGLSP-DGL and/or the sequence p.gamma.zeine-RGLSP-DGL and/or the sequence p.gamma.zeine-RGLSP-DGL-KDEL, selection of the transformed explants on a medium containing kanamycin, production of transformed plants from the abovementioned transformed explants by culture of the latter on suitable media, extraction of the recombinant DGL and/or the polypeptide (.DELTA.54) and/or the polypeptide (.DELTA.4), in particular by grinding seeds produced by the abovementioned transformed plants in a suitable buffer, centrifuging and recovering the supernatant containing the plant extract of enzymatic activity, where appropriate, purification of the recombinant DGL and/or the polypeptide (.DELTA.54) and/or the polypeptide (.DELTA.4) from the extract obtained during the preceding stage, in particular by chromatography carried out on the supernatant, which leads to the preparation of the

recombinant DGL and/or the polypeptide (.DELTA.54) and/or the polypeptide (.DELTA.4) in an essentially pure form.

Detailed Description Text - DETX (63):

The invention more particularly relates to the following plant extracts of enzymatic activity: the extracts of leaves and/or fruits and/or seeds of plants obtained by transformation of explant cells of these plants with the sequence pd35S-RGLSP-DGL or the sequence pd35S-PS-DGL or the sequence pd35S-PPS-DGL, according to one of the processes described above, and containing the recombinant DGL and/or the polypeptide (.DELTA.54) and/or the polypeptide (.DELTA.4), in particular: the extract of tobacco leaves obtained by transformation of explant cells of tobacco leaves with the sequence pd35S-PS-DGL or the sequence pd35S-PPS-DGL, according to the process described above, and containing the polypeptide (.DELTA.54) in combination with the polypeptide (.DELTA.4), the percentage by weight by the mixture of these two polypeptides with respect to the total weight of proteins present in the said extract being from about 0.1 to about 20%, the enzymatic activity of the said extract being from about 100 U/g of FW to about 300 U/g of FW, the extract of tomato leaves or fruits obtained by transformation of explant cells of tomato leaves with the sequence pd35S-PS-DGL, or the sequence pd35S-PPS-DGL, according to the process described above, and containing the polypeptide (.DELTA.54) in combination with the polypeptide (.DELTA.4), the percentage by weight of this mixture of two polypeptides with respect to the total weight of proteins present in the said extract being from about 0.1% to about 20%, the enzymatic activity of the said extract being from about 100 U/g of FW to about 300 U/g of FW, the extract of tobacco leaves obtained by transformation of explant cells of tobacco leaves with the sequence pd35S-RGLSP-DGL, according to the process described above, and containing the polypeptide (.DELTA.4), the percentage by weight of this polypeptide with respect to the total weight of proteins present in the said extract being from about 0.1% to about 20%, the enzymatic activity of the said extract being from about 100 U/g of FW to about 300 U/g of FW, the extract of tobacco seeds obtained by transformation of explant cells of tobacco leaves with the sequence pd35S-PS-DGL or the sequence pd35S-PPS-DGL, according to the process described above, and containing the polypeptide (.DELTA.54), the percentage by weight of the polypeptide (.DELTA.54) with respect to the total weight of proteins present in the said extract being from about 0.1% to about 1%, the enzymatic activity of the said extract being from about 10 U/g of FW to about 300 U/g of FW, the extracts of plant seeds obtained by transformation of explant cells of these plants with the sequence pCRU-PS-DGL or the sequence pCRU-PPS-DGL, or the sequence pGEA1-RGLSP-DGL, or the sequence pGEA6-RGLSP-DGL, according to one of the processes described above, and containing the recombinant DGL and/or the polypeptide (.DELTA.54) and/or the polypeptide (.DELTA.4), in particular: the extract of rape seeds obtained by transformation of explant cells of rape leaves with the sequence pCRU-PS-DGL or the sequence pCRU-PPS-DGL, or the sequence pGEA1-RGLSP-DGL, or the sequence pGEA6-RGLSP-DGL, according to the process described above, and containing the polypeptide (.DELTA.54), the percentage by weight of polypeptide (.DELTA.54) with respect to the total weight of proteins present in the said extract being from about 0.1% to about 1%, the enzymatic activity of the said extract being from about 10 U/g of FW to about 1,000 U/g of FW, the extracts of plant seeds obtained by

transformation of explant cells of these plants with the sequence pAR-IAR-RGLSP-DGL and/or the sequence p.gamma.zeine-RGLSP-DGL, and/or the sequence p.gamma.zeine-RGLSP-DGL-KDEL, according to one of the processes described above, and containing the recombinant DGL and/or the polypeptide (.DELTA.54) and/or the polypeptide (.DELTA.4), in particular: the extract of corn seeds obtained by transformation of explant cells of rape leaves with the sequence pAR-IAR-RGLSP-DGL and/or the sequence p.gamma.zeine-RGLSP-DGL, and/or the sequence p.gamma.zeine-RGLSP-DGL-KDEL, according to the process described above, and containing the polypeptide (.DELTA.54), the percentage by weight of polypeptide (.DELTA.54) with respect to the total weight of proteins present in the said extract being from about 0.1% to about 1%, the enzymatic activity of the said extract being from about 10 U/g of FW to about 1,000 U/g of FW.

Detailed Description Text - DETX (69):

The invention also relates to the polypeptide (.DELTA.54) and the polypeptide (.DELTA.4) obtained by purification of the enzymatic extract of plant leaves and/or seeds and/or fruits, notably solanaceae, such as transformed tobacco or tomato, themselves obtained from plant cells transformed with the sequence pd35S-PS-DGL or the sequence pd35S-PPS-DGL, or the sequence pd35S-RGLSP-DGL, according to the process described above, the said recombinant polypeptides (.DELTA.54) and (.DELTA.4) having a lipase activity as described above.

Detailed Description Text - DETX (70):

The invention also relates to the polypeptide (.DELTA.54) obtained by purification of the enzymatic extract of tobacco seeds, or that of rape seeds, these seeds originating, respectively, from transformed tobacco or rape plants, themselves obtained, respectively, from tobacco or rape cells transformed with the sequence pCRU-PS-DGL or the sequence pCRU-PPS-DGL, according to the processes described above, the recombinant polypeptide (.DELTA.54) having a lipase activity as described above.

Detailed Description Text - DETX (128):

The structural promoter of the nos gene which codes for nopaline synthase (Depicker et al., 1982), the sequence which codes for the nptII gene which codes for neomycin phosphotransferase II (Berg and Berg, 1983) deleted from the region of the first 8 codons, of which the initiator codon is methionine ATG, and fused to the sequence of the first 14 codons of the sequence which codes for the nos gene (Depicker et al., 1982), the sequence which codes for the nos gene devoid of the region of the first 14 codons, the nos terminator (Depicker et al., 1982), a region containing multiple cloning sites (also called polylinker) (HindIII-XbaI-SacI-HpaI-KpnI-ClaI-BglII) preceding the cat gene which codes for chloramphenicol acetyltransferase (Close and Rodriguez, 1982) and the terminal sequences of the gene 6 of the plasmid pTiA6 of Agrobacterium tumefaciens (Liu et al., 1993). To eliminate virtually all the sequence which codes for the cat gene, the plasmid pGA492 was digested twice by SacI (restriction site of the polylinker) and by Scal (restriction site present in the sequence of the cat gene) and then subjected to the action of the enzyme T4 DNA polymerase (New England Biolabs) in accordance with the manufacturer's instructions. The ligation of the modified plasmid (ng) was carried out in a



reaction medium of 10 .mu.l comprising 1 .mu.l of the buffer T4 DNA ligase.times.10 (Amersham); 2.5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria *Escherichia coli* DH5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 12 .mu.g/ml of tetracycline, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. The HindIII restriction site of the plasmid DNA of the clone retained was then modified into an EcoRI restriction site with the aid of an phosphorylated HindIII-EcoRI adaptor (Stratagene Cloning Systems). To carry out this modification, 500 ng of plasmid DNA of the clone retained were digested by HindIII, dephosphorylated by the alkaline phosphatase enzyme of the intestine of the calf (Boehringer Mannheim) in accordance with the manufacturer's instructions and coprecipitated in the presence of 1,500 ng of the HindIII-EcoRI DNA adaptor, 1/10 volume of 3M sodium acetate, pH 4.8, and 2.5 volumes of to absolute ethanol at -80.degree. C. for min. After centrifugation at 12,000 g for min, the DNA precipitated was washed with 70% ethanol, dried, taken up in 8 .mu.l of water, kept at 65.degree. C. for min and then ligated in the presence of 1 .mu.l of the buffer T4 DNA ligase.times.10 (Amersham) and 2.5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. After inactivation of the T4 DNA ligase at 65.degree. C. for min, the ligation reaction mixture was digested by EcoRI, purified by electrophoresis over 0.8% agarose gel, electroeluted (Sambrook et al., 1989), precipitated in the presence of 1/10 volume of 3M sodium acetate, pH 4.8, and 2.5 volumes of absolute ethanol at -80.degree. C. for min, centrifuged at 12,000 g for 30 min, washed with 70% ethanol, dried and then ligated as described above. The bacteria *Escherichia coli* DH5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 12 .mu.g/ml of tetracycline, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by HindIII and EcoRI in particular. The resulting binary plasmid, which only has the last 9 codons of the sequence which codes for the cat gene and of which the EcoRI site is unique, was called pBIOC4.

#### Detailed Description Text - DETX (129):

The expression cassette made up of the promoter pd35S and the terminator polyA 35S was isolated using the plasmid pJIT163.DELTA.. The plasmid pJIT163.DELTA. is derived from the plasmid pJIT163, which itself is derived from the plasmid pJIT60 (Guerineau and Mullineaux, 1993). The plasmid pJIT163 possesses an ATG codon between the HindIII and Sall sites of the polylinker. To suppress this ATG and to obtain the plasmid pJIT163.DELTA., the plasmid pJIT163 DNA was digested twice by HindIII and Sall, purified by electrophoresis over 0.8% agarose gel, electroeluted (Sambrook et al., 1989), precipitated in the presence of 1/10 volume of 3M sodium acetate, pH 4.8, and 2.5 volumes of absolute ethanol at -80.degree. C for min, centrifuged at 12,000 g for 30 min, washed with 70% ethanol, dried, subjected to the action of Klenow enzyme (New England Biolabs) in accordance with the manufacturer's instructions, deproteinated by extraction with 1 volume of phenol:chloroform:isoamyl alcohol (25:24:1) and then 1 volume of chloroform:isoamyl alcohol (24:1), precipitated in the presence of 1/10 volume of 3M sodium acetate, pH 4.8, and 2.5 volumes of absolute ethanol at -80.degree. C for 30 min, centrifuged at 12,000 g for 30 min, washed with 70% ethanol, dried and, finally, ligated in the presence of 1 .mu.l of the buffer T4 DNA ligase.times.10 (Amersham) and 2.5 U of the enzyme

T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria *Escherichia coli* DH5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 50 .mu.g/ml of ampicillin, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. To isolate the expression cassette made up of the promoter pd35S and the terminator polyA 35S (Sacl-XhoI fragment), the plasmid DNA of the clone pJIT163.DELTA. retained was digested by SacI and XhoI. The SacI-XhoI fragment, carrying the expression cassette, was purified by electrophoresis over 0.8% agarose gel, electroeluted (Sambrook et al., 1989), precipitated in the presence of 1/10 volume of 3M sodium acetate, pH 4.8, and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 min, centrifuged at 12,000 g for 30 min, washed with 70% ethanol, dried and then subjected to the action of Mung Bean Nuclease enzyme (New England Biolabs) in accordance with the manufacturer's instructions. This purified insert (200 ng) was cloned in the plasmid DNA of pBIOC4 (20 ng), which had been digested by EcoRI, treated with the enzyme Mung Bean Nuclease and dephosphorylated by the alkaline phosphatase enzyme of the intestine of the calf (Boehringer Mannheim) in accordance with the manufacturer's instructions. The ligation reaction was carried out in 20 .mu.l in the presence of 2 .mu.l of the buffer T4 DNA ligase.times.10 (Amersham), 2 .mu.l of 50% polyethylene glycol 8000 and 5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria *Escherichia coli* Dh5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 12 .mu.l/ml of tetracycline, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. The resulting plasmid was called pBIOC21.

Detailed Description Text - DETX (130):

Dog gastric lipase (DGL) is synthesized naturally in the form of a precursor. The mature DGL protein is made up of 379 amino acids. The complementary DNA of DGL was cloned at the BglII and SalI sites of the expression vector pRU303, leading to the vector pDGL5.303 described in the international application no. WO 94/13816. It was used for construction of the binary plasmids pBIOC25, containing PS-DGL, and pBIOC26, containing **PPS-DGL**, **where the sequence** which codes for the mature DGL is preceded by that which codes for a signal peptide (PS) or a prepropeptide (PPS, that is to say a signal peptide followed by N-terminal vacuole-directing sequences) of plant origin respectively. The PS and **PPS sequences**, made up, respectively, of 23 and 37 amino acids, are those of a reserve protein of the tuberous roots of the sweet potato: sporamin A (Murakami et al., 1986; Matsukoa and Nakamura, 1991).

Detailed Description Text - DETX (131):

To simplify fusions between the sequence of mature DGL and that of the directing signals, PS or PPS, the plasmid pDGL5.303 was modified by introduction of a supplementary HindIII restriction site into the fourth and fifth codons of the mature DGL sequence by mutagenesis directed by PCR using 2 oligodeoxynucleotides, 5' caggagatc TTG TTT GGA AAG CTT CAT CCC 3'(SEQ ID NO: 10) (containing the unique BglII site in the plasmid and providing the supplementary HindIII site) and 5' CAT ATT CCT CAG CTG GGT ATC 3'(SEQ ID NO: 11) (containing the unique PvuII site in the plasmid). Amplification of the

BglII-PvuII fragment by PCR was carried out in 100 .mu.l of reaction medium comprising 10 .mu.l of the buffer Taq DNA polymerase.times.10 (500 mM KCl, 100 mM Tris-HCl, pH 9.0, and 1% Triton.times.100), 6 .mu.l of 25 mM MgCl.sub.2, 3 .mu.l of 10 mM dNTP (dATP, dCTP, dGTP and dTTP), 100 pM of each of the 2 oligodeoxynucleotides described above, 5 ng of matrix DNA (expression vector pRU303 including the complementary DNA of DGL), 2.5 U of Taq DNA polymerase (Promega) and 2 drops of vaseline oil. The DNA was denatured at 94.degree. C. for 30 min, subjected to 30 cycles, each of 1 min of denaturation at 94.degree. C., 1 min of hybridization at 50.degree. C. and 1 min of elongation at 72.degree. C., and then elongation at 72.degree. C. was continued for min. This PCR reaction was carried out in the "DNA Thermal Cycler" machine of PERKIN ELMER CETUS. The oil was removed by extraction with chloroform. The DNA fragments contained in the reaction medium were then precipitated in the presence of 1/10 volume of 3M sodium acetate, pH 4.8, and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 min, centrifuged at 12,000 g for 30 min, washed with 70% ethanol, dried and digested by the 2 restriction enzymes BglII and PvuII. The digested DNA fragments originating from the PCR were purified by electrophoresis over 2% agarose gel, electroeluted (Sambrook et al., 1989), precipitated in the presence of 1/10 volume of 3M sodium acetate, pH 4.8, and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 min, centrifuged at 12,000 g for 30 min, washed with 70% ethanol, dried and then ligated to the plasmid DNA of the vector pDGL5.303, which had been digested twice by BglII and PvuII, purified by electrophoresis over 0.8% agarose gel, electroeluted, subjected to precipitation in alcohol, dried and dephosphorylated by the alkaline phosphatase enzyme of the intestine of the calf (Boehringer Mannheim) in accordance with the manufacturer's instructions. The ligation was carried out with 100 ng of the dephosphorylated vector described above and 50 ng of the digested DNA fragments, originating from the amplification by PCR, described above in a reaction medium of 10 .mu.l in the presence of 1 .mu.l of the buffer T4 DNA ligase.times.10 (Amersham) and 2.5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria Escherichia coli Dh5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 50 .mu.g/ml of ampicillin, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. The plasmid DNA of some of the clones retained was verified by sequencing with the aid of the T7.TM. sequencing kit, marketed by Pharmacia, by the dideoxynucleotide method (Sanger et al., 1977). Introduction of this HindIII restriction site does not modify the genetic code of the DGL. In fact, the natural DGL sequence AAA TTA (Lys-Leu) becomes AAG CTT (Lys-Leu). The resulting plasmid was called pBIOC22 and includes the sequence of the mature DGL protein corresponding to:

#### Detailed Description Text - DETX (133):

The plasmid pBIOC22 was digested totally by BglII and partly by HindIII in order to suppress the sequence which codes for the polypeptide Leu-Phe-Gly-Lys (first 4 amino acids) of the mature DGL protein. This sequence was replaced by that which codes for the signal peptide PS of 23 amino acids (ATG AAA GCC TTC ACA CTC GCT CTC TTC TTA GCT CTT TCC CTC TAT CTC CTG CCC AAT CCA GCC CAT TCC)

(SEQ ID NO: 14) fused to that of the first 4 codons of the sequence which codes for the mature DGL protein ("PS-first 4 codons of mature DGL"). The sequence

"PS-first 4 codons for mature DGL" was amplified by PCR using the plasmid pMAT103 (Matsuoka and Nakamura, 1991) with the aid of the 2 following oligodeoxynucleotides 5' caggagatctgATG AAA GCC TTC ACA CTC GC 3'(SEQ ID NO: 15) and 5' ATG AAG CTT TCC AAA CAA GGA ATG GGC TGG ATT GGG CAG G 3'(SEQ ID NO:

16), in accordance with the protocol of PCR amplification described above in paragraph I. After double enzymatic digestion by BgIII and HindIII, the DNA fragments originating from the PCR amplification were purified by electrophoresis over 2% agarose gel, electroeluted (Sambrook et al., 1989), precipitated in the presence of 1/10 volume of 3M sodium acetate, pH 4.8, and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 min, centrifuged at 12,000 g for 30 min, washed with 70% ethanol, dried and then ligated to the plasmid DNA of pBIOC22, which had been doubly digested by BgIII and HindIII, purified by electrophoresis over 0.8% agarose gel, electroeluted (Sambrook et al., 1989), subjected to precipitation with alcohol, dried and dephosphorylated by the alkaline phosphatase enzyme of the intestine of the calf (Boehringer Mannheim) in accordance with the manufacturer's instructions. The ligation was carried out with 100 ng of the dephosphorylated vector described above and 50 ng of the digested DNA fragments, originating from the PCR amplification, described above in a reaction medium of 10 .mu.l in the presence of 1 .mu.l of the buffer T4 DNA ligase.times.10 (Amersham) and 2.5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria Escherichia coli DH5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 50 .mu.g/ml of ampicillin, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. The plasmid DNA of some of the clones retained was verified by sequencing with the aid of the T7.TM. sequencing kit, marketed by Pharmacia, by the dideoxynucleotide method (Sanger et al., 1977). The sequences of the PS and the mature DGL were cloned, maintaining their open-reading frames. The cleavage sequence between the sequences of the PS and the mature DGL is Ser-Leu. The resulting plasmid was called pBIOC23. Starting from pBIOC23, the BgIII-XbaI fragment carrying the sequence of PS-DGL was isolated by double enzymatic digestion by BgIII and XbaI, purification by electrophoresis over 0.8% agarose gel, electroelution (Sambrook et al., 1989), precipitation with alcohol and drying. This DNA fragment was then treated with Klenow enzyme in accordance with the manufacturer's instructions and ligated to the plasmid DNA of pBIOC21, which had been digested at the HindIII site, treated with Klenow and dephosphorylated by the alkaline phosphatase enzyme of the intestine of the calf (Boehringer Mannheim) in accordance with the manufacturer's instructions. The ligation was carried out with 20 ng of the dephosphorylated vector described above and 200 ng of DNA fragments, containing the PS-DGL, described above in a reaction medium of 20 .mu.l in the presence of 2 .mu.l of the buffer T4 DNA ligase.times.10 (Amersham), 2 .mu.l of 50% polyethylene glycol 8000 and 5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria Escherichia coli DH5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 12 .mu.g/ml of tetracycline, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. The resulting clone was called pBIOC25. The nucleotide sequence of the fragment which codes for the recombinant protein PS-DGL was verified by sequencing with the aid of the T7.TM. sequencing kit, marketed by Pharmacia, by the dideoxynucleotide method (Sanger et al., 1977). The plasmid DNA of the

binary vector pBIOC25 was introduced by direct transformation into the strain LBA4404 of *Agrobacterium tumefaciens* in accordance with the process of Holsters et al. (1978). The validity of the clone retained was verified by enzymatic digestion of the plasmid DNA introduced.

Detailed Description Text - DETX (135):

The plasmid pBIOC22 was digested totally by BglII and partly by HindIII in order to suppress the sequence which codes for the polypeptide Leu-Phe-Gly-Lys (first 4 amino acids) of the mature DGL protein. This sequence was replaced by that which codes for the signal peptide PS of 23 amino acids (ATG AAA GCC TTC ACA CTC GCT CTC TTC TTA GCT CTT TCC CTC TAT CTC CTG CCC AAT CCA GCC CAT TCC AGG TTC AAT CCC ATC CGC CTC CCC ACC ACA CAC GAA CCC GCC) (SEQ ID NO: 17) fused to that of the first 4 codons of the sequence which codes for the mature DGL protein ("PPS-first 4 codons of mature DGL"). The sequence "PPS-first 4 codons for mature DGL" was amplified by PCR using the plasmid pMAT103 (Matsuoka and Nakamura, 1991) with the aid of the 2 following oligodeoxynucleotides 5' caggagatctgATG AAA GCC TTC ACA CTC GC 3' (SEQ ID NO: 15) and 5' ATG AAG CTT TCC AAA CAA GGA GGG TTC GTG TGT GGT TG 3' (SEQ ID NO: 18), in accordance with the protocol of PCR amplification described above in paragraph I. After double enzymatic digestion by BglII and HindIII, the DNA fragments originating from the PCR amplification were purified by electrophoresis over 2% agarose gel, electroeluted (Sambrook et al., 1989), precipitated in the presence of 1/10 volume of 3M sodium acetate, pH 4.8, and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 min, centrifuged at 12,000 g for 30 min, washed with 70% ethanol, dried and then ligated to the plasmid DNA of pBIOC22, which had been doubly digested by BglII and HindIII, purified by electrophoresis over 0.8% agarose gel, electroeluted, subjected to precipitation with alcohol, dried and dephosphorylated by the alkaline phosphatase enzyme of the intestine of the calf (Boehringer Mannheim) in accordance with the manufacturer's instructions. The ligation was carried out with 100 ng of the dephosphorylated vector described above and 50 ng of the digested DNA fragments, originating from the PCR amplification, described above in a reaction medium of 10 .mu.l in the presence of 1 .mu.l of the buffer T4 DNA ligase.times.10 (Amersham) and 2.5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria *Escherichia coli* Dh5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 50 .mu.g/ml of ampicillin, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes.

Detailed Description Text - DETX (136):

The plasmid DNA of some of the clones retained was verified by sequencing with the aid of the T7.TM. sequencing kit, marketed by Pharmacia, by the dideoxynucleotide method (Sanger et al., 1977). The sequences of the PPS and the mature DGL were cloned, maintaining their open-reading frames. The cleavage sequence between the two sequences is Ala-Leu. The resulting plasmid was called pBIOC24. Starting from pBIOC24, the BglII-XbaI fragment carrying the sequence of PPS-DGL was isolated by double enzymatic digestion by BglII and XbaI, purified by electrophoresis over 0.8% agarose gel, electroeluted (Sambrook et al., 1989), precipitated with alcohol and dried. This DNA

fragment was then treated with Klenow enzyme in accordance with the manufacturer's instructions and ligated to the plasmid DNA of pBIOC21, which had been digested at the HindIII site, treated with Klenow and dephosphorylated by the alkaline phosphatase enzyme of the intestine of the calf (Boehringer Mannheim) in accordance with the manufacturer's instructions. The ligation was carried out with 20 ng of the dephosphorylated vector described above and 200 ng of DNA fragments, containing the PPS-DGL, described above in a reaction medium of 20 .mu.l in the presence of 2 .mu.l of the buffer T4 DNA ligase.times.10 (Amersham), 2 .mu.l of 50% polyethylene glycol 8000 and 5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria *Escherichia coli* DH5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 12 .mu.g/ml of tetracycline, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. The resulting clone was called pBIOC26. The nucleotide sequence of the fragment which codes for the recombinant protein PPS-DGL was verified by sequencing with the aid of the T7.TM. sequencing kit, marketed by Pharmacia, by the dideoxynucleotide method (Sanger et al., 1977). The plasmid DNA of the binary vector pBIOC26 was introduced by direct transformation into the strain LBA4404 of *Agrobacterium tumefaciens* in accordance with the process of Holsters et al. (1978). The validity of the clone obtained was verified by enzymatic digestion of the plasmid DNA introduced.

#### Detailed Description Text - DETX (139):

Alignment of the polypeptide sequences of dog gastric lipase and of the precursor of rabbit gastric lipase has demonstrated that the sequence LFGK is present in the two proteins. In the polypeptide sequence of the rabbit lipase determined from the purified natural protein (Moreau et al., 1988), the first three residues L, F and G are absent and form part of the signal peptide of 22 amino acids of RGL. As a result, the signal peptide of rabbit gastric lipase devoid of these three common amino acids was fused to the mature protein sequence of dog gastric lipase. Its polypeptide sequence is made up of the following 19 amino acids: MWVLFMVAALLSALGTTHG (SEQ ID NO: 19). The plasmid pBIOC22 was thus digested totally by BhlII and partly by HindIII in order to suppress the sequence which codes for the polypeptide Leu-Phe-Gly-Lys (first 4 amino acids) of the mature DGL protein. This sequence was replaced by that which codes for the signal peptide RGLSP of rabbit gastric lipase of 19 amino acids (ATG TGG GTG CTT TTC ATG GTG GCA GCT TTG CTA TCT GCA CTT GGA ACTACA CAT

GGT) (SEQ ID NO: 20) fused to that of the first 4 codons of the mature DGL protein ("RGLSP-first 4 codons of mature DGL"). The sequence "RGLSP-first 4 codons of mature DGL" was amplified by PCR using the plasmid pJO101 with the aid of the 2 following oligodeoxynucleotides 5' aggagatctcaacaATG TGG GTG CTT TTC ATG GTG 3' (SEQ ID NO: 21) and 5' G ATG AAG CTT TCC AAA CAA ACC ATG TGT AGT

TCC AAG TG 3' (SEQ ID NO: 22), in accordance with the protocol of PCR amplification described above in paragraph I. After double enzymatic digestion by BglII and HindIII, the DNA fragments originating from the PCR amplification were purified by electrophoresis over 2% agarose gel, electroeluted (Sambrook et al., 1989), precipitated in the presence of 1/10 volume of 3M sodium acetate, pH 4.8, and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 min, centrifuged at 12,000 g for 30 min, washed with 70% ethanol, dried and

then ligated to the plasmid DNA of pBIOC22, which had been doubly digested by BglII and HindIII, purified by electrophoresis over 0.8% agarose gel, electroeluted (Sambrook et al., 1989), subjected to precipitation with alcohol, dried and dephosphorylated by the alkaline phosphatase enzyme of the intestine of the calf (Boehringer Mannheim) in accordance with the manufacturer's instructions. The ligation was carried out with 100 ng of the dephosphorylated vector described above and 50 ng of the digested DNA fragments, originating from the PCR amplification, described above in a reaction medium of 10  $\mu$ l in the presence of 1  $\mu$ l of the buffer T4 DNA ligase.times.10 (Amersham) and 2.5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria Escherichia coli DH5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on a medium containing 50  $\mu$ g/ml of ampicillin, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. The plasmid DNA of some of the clones retained was verified by sequencing with the aid of the T.sub.7.TM. sequencing kit, marketed by Pharmacia, by the dideoxynucleotide method (Sanger et al., 1977). The sequences of the RGLSP and the mature DGL were cloned, maintaining their open reading frames (that is to say such that they constitute a unique open reading frame). The cleavage sequence between the sequences of the RGLSP and the mature DGL is Gly-Leu. The resulting plasmid was called pBIOC40. Starting from pBIOC40, the BglII-XbaI fragment carrying the sequence of RGLSPS-DGL was isolated by double enzymatic digestion by BglII and XbaI, purification by electrophoresis over 0.8% agarose gel, electroelution (Sambrook et al., 1989), precipitation with alcohol and drying. This DNA fragment was then treated with Klenow enzyme in accordance with the manufacturer's instructions and ligated to the plasmid DNA of pBIOC21, which had been digested at the HindIII site, treated with Klenow and dephosphorylated by the alkaline phosphatase enzyme of the intestine of the calf (Boehringer Mannheim) in accordance with the manufacturer's instructions. The ligation was carried out with 20 ng of the dephosphorylated vector described above and 200 ng of DNA fragments, containing the RGLSP-DGL, described above in a reaction medium of 20  $\mu$ l in the presence of 2  $\mu$ l of the buffer T4 DNA ligase.times.10 (Amersham), 2  $\mu$ l of 50% polyethylene glycol 8000 and 5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria Escherichia coli DH5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on a medium containing 12  $\mu$ g/ml of tetracycline, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. The resulting clone was called pBIOC41. The nucleotide sequence of the fragments which code for the recombinant protein RGLSP-DGL was verified by sequencing with the aid of the T7.TM. sequencing kit, marketed by Pharmacia, by the dideoxynucleotide method (Sanger et al., 1977). The plasmid DNA of the binary vector pBIOC41 was introduced by direct transformation into the strain LBA4404 of Agrobacterium tumefaciens in accordance with the process of Holsters et al. (1978). The validity of the clone retained was verified by enzymatic digestion of the plasmid DNA introduced.

#### Detailed Description Text - DETX (149):

Isolation of the BglII-XbaI fragment carrying the **sequence PPS-DGL** using pBIOC24 has already been described in I-A-b. This fragment was ligated to the plasmid DNA of pBIOC28 at the EcoRI site treated with Klenow and

dephosphorylated by the alkaline phosphatase enzyme of the intestine of the calf (Boehringer Mannheim) in accordance with the manufacturer's instructions. The ligation was carried out with 20 ng of the dephosphorylated vector described above and 200 ng of the DNA fragments BglII-XbaI containing PPS-DGL in a reaction medium of 20  $\mu$ l in the presence of the buffer T4 DNA ligase.times.10 (Amersham), 2  $\mu$ l of 50% polyethylene glycol 8000 and 5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria *Escherichia coli* DH5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on a medium containing 12  $\mu$ g/ml of tetracycline, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. The resulting plasmid was called pBIOC29. The nucleotide sequence of the recombinant protein PPS-DGL was verified by sequencing with the aid of the T7.TM. sequencing kit, marketed by Pharmacia, by the dideoxynucleotide method (Sanger et al., 1977). The plasmid DNA of the binary vector pBIOC29 was introduced by direct transformation into the strain LBA4404 of *Agrobacterium tumefaciens* in accordance with the process of Holsters et al. (1978). The validity of the clone retained was verified by enzymatic digestion of the plasmid DNA introduced.

#### Detailed Description Text - DETX (153):

To obtain the binary plasmid pBIOC90 similar to pBIOC21 but in which the promoter p35S was replaced by the promoter pGEA1D, the fragment HindIII-BamHI treated with Klenow, containing the promoter pGEA1, was isolated using plasmid pGUS2-pGEA1. The clone pGUS-2-pGEA1 deriving from pBI221 by replacement of the promoter p35S by the promoter pGEA1, contains 2 ATG in frame: ATG of the gene GEA1 (Em2) and ATG of the gene gus. The ATG of the gene GEA1 was destroyed. The DNA fragment contained between the Sall site and the sequences upstream from the ATG of the gene GEA1 of the clone pGUS-2-pGEA1 was then amplified by PCR using 2 oligonucleotides: 5' CAAACGTGTACAATAGCCC 3' (SEQ ID NO: 23) and 5' CCCGGGGATCCTTTTTTG 3' (SEQ ID NO: 24). The hybridization temperature was adjusted. The fragment amplified by PCR was digested by Sall and BamHI, purified by electrophoresis over 2% agarose gel, electroeluted (Sambrook et al. 1989), precipitated in the presence of 1/10 volume of 3M sodium acetate pH 4.8 and 2.5 volumes of absolute ethanol at -80.degree. C. for minutes, centrifuged at 12000 g for 30 minutes, washed with 70% ethanol, then ligated to plasmid DNA of pGUS-2-GEA1 double digested by Sall and BamHI, purified by electrophoresis over 0.8% agarose gel, electroeluted (Sambrook et al., 1989), subjected to precipitation with alcohol, dried. Ligation was carried out with 100 ng of vector and 50 ng of digested DNA fragments originating from the PCR amplification described above, in a reaction medium of 10  $\mu$ l in the presence of 1  $\mu$ l of the buffer T4 DNA ligase.times.10 (Amersham) and 2.5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria *Escherichia coli* Dh5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 50  $\mu$ g/ml ampicillin, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. Certain retained clones were verified by sequencing with the aid of the T7.TM. sequencing kit, marketed by Pharmacia, by the dideoxynucleotide method (Sanger et al., 1977). The resulting clone was called pGUS-2-pGEA1D.



Detailed Description Text - DETX (161):

The fragment amplified by PCR was digested by *AccI* and *Bam*HI, purified by electrophoresis over 2% agarose gel, electroeluted (Sambrook et al. 1989), precipitated in the presence of 1/10 volume of 3M sodium acetate pH 4.8 and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 minutes, centrifuged at 12000 g for 30 minutes, washed with 70% ethanol, dried, then ligated to plasmid DNA of pGUS-2-GEA6 double digested by *AccI* and *Bam*HI, purified by electrophoresis over 0.8% agarose gel, electroeluted (Sambrook et al., 1989), subjected to precipitation with alcohol, dried. Ligation was carried out with 100 ng of the vector described above and 50 ng of digested DNA fragments originating from the PCR amplification described above, in a reaction medium of 10 .mu.l in the presence of 1 .mu.l of the buffer T4 DNA ligase.times.10 (Amersham) and 2.5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria *Escherichia coli* Dh5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 50 .mu.g/ml ampicillin, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. Certain retained clones were verified by sequencing with the aid of the T7.TM. sequencing kit, marketed by Pharmacia, by the dideoxynucleotide method (Sanger et al., 1977). The resulting clone was called pGUS-2-pGEA6D.

Detailed Description Text - DETX (175):

The sequence which codes for the precursor of HGL was isolated by double digestion with *Pst*I and *Dra*I, purified by electrophoresis over 0.8% agarose gel, electroeluted (Sambrook et al., 1989), precipitated in the presence of 1/10 volume of 3M sodium acetate pH 4.8 and 2.5 volumes of absolute ethanol at minus 80.degree. C. for minutes, centrifuged at 12000 g for 30 minutes, washed with 70% ethanol and dried. Then, it was cloned at the *Pst*I and *Spe*I sites (subjected to the action of the enzyme T4 DNA polymerase (Biolabs) in accordance with the manufacturer's instructions) of the plasmid pBSIISK+ marketed by Stratagene. The ligation was carried out with 100 ng of the vector and 50 ng of the DNA fragments carrying the sequence which codes for the precursor of HGL described above, in a reaction medium of 10 .mu.l in the presence of 1 .mu.l of the buffer T4 DNA ligase.times.10 (Amersham) and 2.5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria *Escherichia coli* DH5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 50 .mu.g/ml of ampicillin, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. The resulting plasmid was called pBIOC83.

Detailed Description Text - DETX (177):

The PCR amplification of the fragment *Pst*I-*Msc*I was carried out in 100 .mu.l of reaction medium containing 10 .mu.l of the buffer Taq DNA polymerase.times.10 (500 mM KCl, 100 mM Tris-HCl, pH 9.0 and 1% Triton.times.100), 6 .mu.l of mM MgCl.sub.2, 3 .mu.l of 10 mM dNTP (dATP, dCTP, dGTP and dTTP), 100 pM of each of the 2 oligodeoxy-nucleotides described above, 5 ng of matrix DNA (vector pBIOC83), 2.5 U of Tag DNA polymerase (Promega) and 2 drops of vaseline oil. The DNA was denatured at 94.degree. C. for 5 minutes, subjected to 30 cycles each constituted by 1 minute of

denaturation at 94.degree. C., 1 minute of hybridization at 65.degree. C. and 1 minute of elongation at 72.degree. C., then elongation at 72.degree. C. was continued for 5 minutes. This PCR reaction was carried out in the "DNA Thermal Cycler" machine of PERKIN ELMER CETUS. The oil was removed by extraction with chloroform. The DNA fragments contained in the reaction medium were then precipitated in the presence of 1/10 volume of 3M sodium acetate, pH 4.8, and 2.5 volumes of absolute ethanol at minus 80.degree. C. for 30 min, centrifuged at 12,000 g for 30 min, washed with 70% ethanol, dried and digested by the 2 restriction enzymes PstI and MscI. The digested DNA fragments originating from the PCR amplification were purified by electrophoresis over 2% agarose gel, electroeluted (Sambrook et al., 1989), precipitated in the presence of 1/10 volume of 3M sodium acetate, pH 4.8, and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 min, centrifuged at 12,000 g for min., washed with 70% ethanol, dried and then ligated to the plasmid DNA of pBIOC83, which had been digested twice by PstI and MscI, purified by electrophoresis over 0.8% agarose gel, electroeluted, subjected to precipitation with alcohol, dried. The ligation was carried out with 100 ng of the vector and 50 ng of the digested DNA fragments, originating from the amplification by PCR, described above, in a reaction medium of 10 .mu.l in the presence of 1 .mu.l of the buffer T4 DNA ligase.times.10 (Amersham) and 2.5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria Escherichia coli Dh5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 50 .mu.g/ml of ampicillin, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. Some of the retained clones were verified by sequencing with the aid of the T7.TM. sequencing kit, marketed by Pharmacia, by the dideoxynucleotide method (Sanger et al., 1977). Introduction of the BamHI restriction site does not modify the genetic code of the HGL. In fact, the natural HGL sequence GGA AGC (Gly-Ser) becomes GGA TCC (Gly-Ser). The resulting plasmid was called pBIOC84.

#### Detailed Description Text - DETX (181):

The plasmid pBIOC84 was digested twice by PstI and BamHI in order to suppress the sequence which codes for the signal peptide HSLSP and the first 8 amino acids of the mature HGL protein (Leu-Phe-Gly-Lys-Leu-His-Pro-Gly). This sequence was replaced by that which codes for the signal peptide HPLSP of 16 amino acids (ATG CTG CCA CTT TGG ACT CTT TCA CTG CTG CTG GGA GCA GTA GCA GGA) (SEQ ID NO: 29) fused to that which codes for the first 8 codons of the mature HGL protein ("HPLSP-first 8 codons of mature HGL"). The sequence "HPLSP-first 8 codons of mature HGL" was amplified by PCR from the matrix 5' aaactgcaggctcgagaacaATG CTG CCA CTT TGG ACT CTT TCA CTG CTG CTG GGA GCA GTA GCA GGA TTG TTT GGA AAA TTA CAT CCT GGA tcc CCT G 3' (SEQ ID NO: 30) using the 2 oligodeoxynucleotides, 5' aaactgcaggctcgagaacaATG C 3' (SEQ ID NO: 31) and 5' C AGG gga TCC AGG ATG TAA TTT TCC 3' (SEQ ID NO: 32), following the PCR amplification protocol described previously (see paragraph I above). The hybridization temperature was adjusted. After double enzymatic digestion by PstI and BamHI, the DNA fragments originating from the PCR amplification were purified by electrophoresis over 2% agarose gel, electroeluted (Sambrook et al. 1989), precipitated in the presence of 1/10 volume of 3M sodium acetate pH 4.8 and 2.5 volumes of absolute ethanol at -80.degree. C. for 30 minutes,

centrifuged at 12000 g for 30 minutes, washed with 70% ethanol, dried, then ligated with plasmid DNA of pBIOC84 double digested by PstI and BamHI, purified by electrophoresis over 0.8% agarose gel, electroeluted (Sambrook et al., 1989), subjected to precipitation with alcohol, dried. Ligation was carried out with 100 ng of vector and 50 ng of digested DNA fragments originating from the PCR amplification described above, in a reaction medium of 10  $\mu$ l in the presence of 1  $\mu$ l of the buffer T4 DNA ligase.times.10 (Amersham) and 2.5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria *Escherichia coli* Dh5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 50  $\mu$ g/ml ampicillin, was extracted by the alkaline lysis method (Birnboim and Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. Certain retained clones were verified by sequencing with the aid of the T7.TM. sequencing kit, marketed by Pharmacia, by the dideoxynucleotide method (Sanger et al., 1977). The sequences of HPLSP and mature HGL were cloned while maintaining their open reading frames (that is to say, such that they constitute a unique open reading frame). The restriction sequence between the sequences HPLSP and mature HGL is Gly-Leu. The resulting plasmid was called pBIOC86.

#### Detailed Description Text - DETX (184):

The plasmid pBIOC84 was double digested by PstI and BamHI in order to suppress the sequence which codes for the signal peptide HGLSP and the first 8 amino acids of the mature HGL protein (Leu-Phe-Gly-Lys-Leu-His-Pro-Gly). This sequence was replaced by that which codes for the signal peptide RGLSP of 19 amino acids (ATG TGG GTG CTT TTC ATG GTG GCA GCT TTG CTA TCT GCA CTT GGA ACT

ACA CAT GGT) (SEQ ID NO: 33) fused to that which codes for the first 8 codons of the mature HGL protein ("RGLSP-first 8 codons of mature HGL"). The sequence "RGLSP-first 8 codons of mature HGL" was amplified by PCR from the matrix 5' aaactgcaggctcgagaacaATG CTG CCA CTT TGG ACT CTT TCA CTG CTG CTG GGA GCA GTA GCA

GGA TTG TTT GGA AAA TTA CAT CCT GGA tcc CCT G 3' (SEQ ID NO: 34) using the 2 oligodeoxynucleotides, 5' aaactgcaggctcgagaacaATG TGG 3' (SEQ ID NO: 35) and 5' C AGG gga TCC AGG ATG TAA TTT TCC 3' (SEQ ID NO: 32), following the PCR amplification protocol described previously (see paragraph I above). The hybridization temperature was adjusted. After double enzymatic digestion by PstI and BamHI, the DNA fragments originating from the PCR amplification were purified by electrophoresis over 2% agarose gel, electroeluted (Sambrook et al. 1989), precipitated in the presence of 1/10 volume of 3M sodium acetate pH 4.8 and 2.5 volumes of absolute ethanol at -80.degree. C. for minutes, centrifuged at 12000 g for 30 minutes, washed with 70% ethanol, dried, then ligated with plasmid DNA of pBIOC84 double digested by PstI and BamHI, purified by electrophoresis over 0.8% agarose gel, electroeluted (Sambrook et al., 1989), subjected to precipitation with alcohol, dried. Ligation was carried out with 100 ng of vector and 50 ng of digested DNA fragments originating from the PCR amplification described above, in a reaction medium of 10  $\mu$ l in the presence of 1  $\mu$ l of the buffer T4 DNA ligase.times.10 (Amersham) and 2.5 U of the enzyme T4 DNA ligase (Amersham) at 14.degree. C. for 16 hours. The bacteria *Escherichia coli* Dh5.alpha., rendered competent beforehand, were transformed (Hanahan, 1983). The plasmid DNA of the clones obtained, selected on 50  $\mu$ g/ml ampicillin, was extracted by the alkaline lysis method (Birnboim and

Doly, 1979) and analysed by enzymatic digestion by restriction enzymes. Certain retained clones were verified by sequencing with the aid of the T7.TM. sequencing kit, marketed by Pharmacia, by the dideoxynucleotide method (Sanger et al., 1977). The sequences of RGLSP and mature HGL were cloned while maintaining their open reading frames (that is to say, such that they constitute a unique open reading frame). The restriction sequence between the sequences RGLSP and mature HGL is Gly-Leu. The resulting plasmid was called pBIOC88.

Detailed Description Text - DETX (291):

1 gram of lyophilized leaves is ground at 4.degree. C. in 30 ml of 20 mM glycine buffer, pH 2.5, and the mixture is stirred gently for 15 minutes. During the steeping, the pH is kept at 2.5 by addition of 1N HCl. The product of the steeping is centrifuged at 15,000 g for 5 minutes. The pH of the supernatant is adjusted to 4 by addition of 1N NaOH. After filtration over MIRACLOTH (Calbiochem), all the supernatant is applied to a cation exchange resin column (S-Sepharose Fast Flow resin--Pharmacia) of 10 ml (diameter 1.6 cm) equilibrated in a buffer of 20 mM sodium acetate, pH 4.0, and 20 mM NaCl at a flow rate of 1 ml per minute. Fractions of 2 ml are collected. After passage of the supernatant, the column is washed with 40 ml of the equilibration buffer. The proteins retained on the column are eluted in accordance with the following protocol: linear gradient in mM sodium acetate buffer, pH 4.0, of 20 mM to 210 mM NaCl in the course of 30 minutes for elution of a first set of peaks of proteins which do not contain lipase activity, the test being carried out on analytical samples of 1 ml, plateau at 210 mM NaCl for 20 minutes, linear gradient in 20 mM sodium acetate buffer, pH 4.0, of 210 mM to 500 mM NaCl in the course of 30 minutes for elution of a second set of peaks. The lipase activity-measured on analytical samples of 0.5 ml is eluted during this second gradient at an ionic strength of between 300 and 400 mM.

Detailed Description Text - DETX (305):

2 grams of lyophilized leaves is ground up at 4.degree. C. in 60 ml of 0.2 M NaCl, pH 3, and the mixture is gently agitated for 15 minutes at 4.degree. C. During this steeping, the pH is kept at 3 by the addition of 1N HCl. The product of the steeping (homogenate) is centrifuged at 10,000 g for 10 minutes. After filtration over MIRACLOTH (Calbiochem) and a 0.45.mu. MILLIPORE filter, all the supernatant is injected into a cation exchange resin column (RESOURCE S 6 ml--Pharmacia--16 mm i.d..times.30 mm) equilibrated in a buffer of 20 mM sodium acetate, 0.2 M NaCl pH 3 at a flow rate of 8 ml/minute (240 cm h-1).

Detailed Description Text - DETX (306):

After passage of the non-retained fraction, the column is washed with 30 times its volume of the equilibration buffer. The proteins retained on the column are eluted with a linear gradient in 20 mM sodium acetate buffer, pH 3, of 0.2 M NaCl to 0.5 M NaCl in 7 column volumes. Fractions of 4 ml are collected.

Detailed Description Text - DETX (320):

The seed extract is dialyzed against a buffer of 10 mM of sodium acetate.

pH4, 140 mM of NaCl, 3 mM of KCl then applied to an immunoaffinity column constituted by dog gastric anti-lipase polyclonal antibodies obtained from guinea-pigs coupled to a resin (hydrazide Avidgel--BIOPROBE INTERNATIONAL, Inc.).

Detailed Description Text - DETX (321):

The resin/seed extract contact is for 30 minutes at 4.degree. C. under gentle agitation. The resin is then rinsed with 10 column volumes of buffer, 10 mM sodium acetate, pH4, 150 mM NaCl, 3 mM KCl. The DGL is eluted with 5 column volumes of buffer, 0.2 M glycine, pH 2.8, 150 mM NaCl. The collected fractions have a volume equal to 1 column volume and contain 1/20th V/V of 1M Tris buffer, pH 9. Analysis by electrophoresis over polyacrylamide gel in denaturing medium shows a protein of molecular weight of about 37 kDa.

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DOCUMENT-IDENTIFIER: US 6489100 B1

TITLE: Microorganisms and methods for overproduction of DAHP by  
cloned PPS gene

DATE-ISSUED: December 3, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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APPL-NO: 09/ 440503

DATE FILED: November 15, 1999

PARENT-CASE:

This is a request for filing a Continuation under 37 C.F.R. .sctn.1.60 of prior Ser. No. 08/801,454 filed on Feb. 18, 1997, now U.S. Pat. No. 5,906,925, and of prior Ser. No. 09/277,183 filed on Mar. 26, 1999, to be issued as U.S. Pat. No. 5,985,617, both of JAMES C. LIAO for MICROORGANISMS AND METHODS FOR OVERPRODUCTION OF DAHP BY CLONED PPS GENE.

US-CL-CURRENT: 435/6, 435/105, 435/108, 435/200, 435/72, 536/23.2  
, 536/23.7, 536/24.1

ABSTRACT:

Genetic elements comprising expression vectors and a gene coding for phosphoenol pyruvate synthase is utilized to enhance diversion of carbon resources into the common aromatic pathway and pathways branching therefrom. The overexpression of phosphoenol pyruvate synthase increases DAHP production to near theoretical yields.

10 Claims, 14 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 6

----- KWIC -----

Abstract Text - ABTX (1):

Genetic elements comprising expression vectors and a gene coding for phosphoenol pyruvate synthase is utilized to enhance diversion of carbon resources into the common aromatic pathway and pathways branching therefrom.

The overexpression of phosphoenol pyruvate synthase increases DAHP production to near theoretical yields.

TITLE - TI (1):

Microorganisms and methods for overproduction of DAHP by cloned **PPS gene**

Parent Case Text - PCTX (1):

This is a request for filing a Continuation under 37 C.F.R. .sctn.1.60 of prior Ser. No. 08/801,454 filed on Feb. 18, 1997, now U.S. Pat. No. 5,906,925, and of prior Ser. No. 09/277,183 filed on Mar. 26, 1999, to be issued as U.S. Pat. No. 5,985,617, both of JAMES C. LIAO for MICROORGANISMS AND METHODS FOR OVERPRODUCTION OF DAHP BY CLONED **PPS GENE**.

Brief Summary Text - BSTX (18):

The present invention provides genetically engineered strains of microorganisms that overexpress the **pps gene** for increasing the production of DAHP to near theoretical yields. The present invention also provides genetically engineered strains of microorganisms where at least one of the plasmids pPS341, pPSL706, pPS706, or derivatives thereof is transformed into a microorganism for increasing the production of DAHP to near theoretical yields.

Brief Summary Text - BSTX (19):

The present invention further provides a method for increasing carbon flow for the biosynthesis of DAHP in a host cell comprising the steps of transforming into the host cell recombinant DNA comprising a **pps gene so that Pps** is expressed at enhanced levels relative to wild type host cells, concentrating the transformed cells through centrifugation, resuspending the cells in a minimal, nutrient lean medium, fermenting the resuspended cells, and isolating DAHP from the medium.

Brief Summary Text - BSTX (20):

The present invention further provides methods of increasing carbon flow into the common aromatic pathway of a host cell comprising the step of transforming the host cell with recombinant DNA comprising a **pps gene so that Pps** is expressed at appropriate point in the metabolic pathways at enhanced levels relative to wild type host cells.

Brief Summary Text - BSTX (24):

The present invention further provides a genetic element comprising a **pps gene** and one or more genes selected from the group consisting of an aroF gene, aroG gene, aroH gene, and an aroB gene.

Brief Summary Text - BSTX (25):

The present invention further provides a DNA molecule comprising a vector carrying a **gene coding for Pps**.

Detailed Description Text - DETX (3):

The inventor have found that cell lines can be developed that increase the carbon flux into DAHP production and achieve near theoretical yields of DAHP by overexpressing phosphoenolpyruvate synthase (Pps) in the cell lines. Overexpression of Pps can increase the final concentration and yield of DAHP by as much as two-fold, to a near theoretical maximum as compared to wild type cell lines. The overexpression of Pps is achieved by transforming a cell line with recombinant DNA comprising a pps gene so that Pps is expressed at enhanced level relative to the wild type cell line and so that the yield of DAHP approaches its theoretical value.

Detailed Description Text - DETX (5):

Besides the use of the pps gene, the present invention also provides for transfer of genetic elements comprising the tkt gene, the gene coding for DAHP synthase (aroF in E. coli), the gene coding for 3-dehydroquinate synthase (aroB in E. coli), or other genes encoding enzymes that catalyze reactions in the common aromatic pathway. Such a cell transformation can be achieved by transferring one or more plasmids that contain genes that code for enzymes that increase the carbon flux for DAHP synthesis and for subsequent synthesis of other desired cyclic, pre-aromatic, and aromatic metabolites. As a result of this transfer of genetic element(s), more carbon enters and moves through the common aromatic pathway relative to wild type host cells not containing the genetic elements of the present invention.

Detailed Description Text - DETX (6):

In one embodiment, the present invention comprises a method for increasing carbon flow into the common aromatic pathway of a host cell by increasing the production of DAHP through the overexpression of Pps at the appropriate point in the common aromatic pathway to provide additional PEP at the point where PEP condenses with E4P. Increasing carbon flow requires the step of transforming the host cell with recombinant DNA containing a pps gene so that Pps is overexpressed at enhanced levels relative to wild type host cells. DAHP is then produced by fermentation of the transformed cell in a nutrient medium where the DAHP can be extracted from the medium on a batch wise or continuous extraction procedure.

Detailed Description Text - DETX (7):

In another embodiment, the present invention involves the co-overexpression of a pps gene and other genes coding for enzymes of the common aromatic pathway where additional genetic material is transformed into the host cell. The genes transferred can include the tkt gene, DAHP synthase gene and DHQ synthase gene (preferably the aroF or aroB genes, respectively). Although the work so far has centered around transforming certain host cell strains of E. coli such as AB2847 aroB, this particular host cell may not be the preferred host cells for the commercial production of DAHP or DAHP metabolites through the overexpression of Pps.



Detailed Description Text - DETX (8):

Another embodiment of the present invention is a method for enhancing a host cell's biosynthetic production of compounds derived from the common aromatic pathway. This method involves the step of increasing expression of Pps in the host cell relative to a wild type host cell. The step of increasing expression of Pps can include transferring into the host cell a vector carrying the pps gene. The overexpression of Pps results in forcing increased carbon flow into the biosynthesis of DAHP.

Detailed Description Text - DETX (9):

In another embodiment of the present invention, a method for enhancing a host cell's biosynthetic production of compounds derived from the common aromatic pathway relative to wild type host cell's biosynthetic production of such compound is provided. This method requires the step of increasing expression in a host cell of a protein catalyzing conversion of pyruvate to PEP. The expression of such a protein can involve transferring into the host cell recombinant DNA including a pps gene.

Detailed Description Text - DETX (10):

In another preferred embodiment, the present invention comprises a genetic element comprising the pps gene and a gene selected from the group consisting of a *aroF* gene, a *aroB* gene, and a *tkt* gene. Such a genetic element can comprise plasmid pPS341, a vector carrying a pps gene.

Detailed Description Text - DETX (50):

In previous work, the inventor demonstrated that overexpression of Pps in host cells cultured on nutrient rich, glucose containing medium led to growth inhibition, increased glucose consumption, and excretion of pyruvate and acetate. Their previous study also showed that the effects of Pps overexpression on DAHP production, in actively growing cultures, are not as significant, and that the adverse effects of Pps overexpression on cell growth negated any beneficial effects on DAHP production.

Detailed Description Text - DETX (54):

PEP is also a precursor to the pathways that utilize the Ppc enzyme coded by the *ppc* gene. It has been reported that the deletion of *ppc* increased the production of phenylalanine and acetate. Moreover, it has been shown that the overexpression of Ppc in a wild-type host reduces acetate production. Both results may indicate that the flux through Ppc (from PEP to OAA) is reasonably significant under those conditions, and thus, the modulation of Ppc expression level may affect the utilization of PEP. However, in the present invention, deleting the chromosomal *ppc* gene did not have a positive effect on DAHP production, suggesting that the flux through Ppc is not important in the methods of the present invention.

Detailed Description Text - DETX (55):

One preferred embodiment of the present invention encompasses modification of a host cell to cause overexpression of an enzyme having the catalytic

properties of naturally derived Pps, and, thereby maximizing the yield of DAHP to near theoretical yields. Enzymes having the catalytic activity of Pps include, but are not limited to, Pps produced by expression in whole cells of a naturally derived pps gene, enzymes produced by expression in whole cells of a naturally derived pps gene modified by sequence deletion or addition so that the expressed enzyme has an amino acid sequence that varies from unmodified Pps, abzymes produced to have catalytic sites with steric and electronic properties corresponding to catalytic sites of Pps, or other proteins produced to have the capability of catalyzing the conversion of pyruvate to PEP by any other art recognized means.

Detailed Description Text - DETX (57):

Additionally, the transformation of DNA, including the pps gene, into microorganisms engineered for the overexpression of other substrates, and/or overexpression or derepression of enzymes in the pentose phosphate or common aromatic pathway can be used to tailor the microorganism to achieve near theoretical yields of such DAHP metabolites as tyrosine, tryptophan, phenylalanine, and other aromatic metabolites such as indigo, catechol and quinoid organics such as quinic acid, benzoquinone, and hydroquinone.

Detailed Description Text - DETX (72):

Plasmid pPS341 was constructed by cloning a fragment of E. coli chromosomal DNA containing pps gene into an IPTG-inducible expression vector pUHE23-2 (a pBR322 derivative) as taught by Patnaik et al., and the contents of which are herein incorporated by reference. Plasmid pPS341X1 containing the inactive gene product of pps was constructed by codon insertion mutagenesis, the details of which are fully described in Patnaik et al. The pps gene on pPS341 was inserted with a Mu dII1734 lac.sup.+ Km.sup.r (MudK) according to published protocol of Castiño et al., the contents of which are herein incorporated by reference. Briefly, a Mu lysate was made from a donor strain POII1734/pPS341, which was lysogenized by the mini-Mu element and a Mu cts. The lysate was used to infect a Mu lysogen of HG4 pps pck, and colonies were selected for Ap.sup.r and Km.sup.r simultaneously to ensure that the mini-Mu element hopped to the plasmid. Colonies were further screened for Pps.sup.- phenotype (inability to grow on pyruvate). Restriction analysis of plasmid DNA further confirmed the insertion of the MudK element into the pps gene on plasmid pPS341. 20% of these selected colonies showed IPTG-dependent expression of .beta.-galactosidase, indicating an in-frame insertion. Plasmid from one such colony was named pPS1734, which was then linearized at the Scal site, and then transformed into strain JC7623 recB21 recC22 sbcB15. Transformants were selected for Km.sup.r and scored for Ap sensitivity. Such colonies presumably contained pps::MudK on the chromosome. By use of P1 transduction, this locus was moved to AB2847 and Km.sup.r transductants were further screened for inability to grow on pyruvate. One such colony was designated JCL1362 and used for later studies. The MudK insertion into chromosomal pps was further confirmed by cotransduction frequency (89%) with Tet.sup.r marker from strain CAG12151 zdh-925::Tn10.

Detailed Description Text - DETX (75):

The plasmid pPS706 was constructed by inserting a 2.4 kb PCR fragment containing the promoter-less pps gene into the vector pJF118EH. The primers were designed from the published pps sequence and contained an EcoRI site and a .phi.10 ribosome binding site upstream of the pps sequence and a BainzHI site downstream of the sequence. The PCR product was then cloned into the EcoRI and BaZizHI sites of pJF118EH. Positive clones were selected based on complementation of HG4 pps for growth on pyruvate. Expression of pps from this construct is controlled by the tac promoter inducible by IPTG.

Detailed Description Text - DETX (76):

The plasmid pPSL706 was then constructed from pPS706 as shown in FIG. 5. Briefly, a Scal/EcoRI fragment containing the pps gene was cut from pPS706 and purified from the restriction buffer. This fragment was then cloned into a purified Scal-EcoRI fragment containing the luxI' promoter from pGS103, kindly given to the inventor by Tom Baldwin. Department of Biochemistry and Biophysics, Texas A&M University. Expression using this system is controlled by the autoinducer (AI) in the culture media. pPSL706 is ampicillin resistant and compatible with other pACYC184 derivatives such as pRWS and pATI. The strains and plasmids used are summarized in Table I and Table II.

Detailed Description Text - DETX (88):

To gain insight into the metabolic flux distribution, the culture broth was analyzed for fermentation byproducts by use of HPLC. Samples were taken from cultures in glucose media with varying activities of Pps, AroG, and TktA. Results indicate that the host strain AB2847 produced acetate, succinate, and formate as the major byproducts when neither AroG nor Pps was overexpressed. Production of these acids generally decreased with the increase in IPTG concentration, except formate. This decrease correlates with the increase in DAHP production. When AB2847/pAT1/pPS706 was cultured in glucose with IPTG concentration beyond 50 mM, the broth had undetectable levels of these acids (data not shown). While levels of formic and acetic acid decreased with increase in Pps activity, succinic acid either remained constant (0 .mu.M IPTG) or increased (10.50 .mu.M IPTG) with an increase in Pps activity. This increase could be contributed to Pps induced increase in PEP level, which is spilled over through PEP carboxylase and eventually to succinate.

Detailed Description Text - DETX (91):

This example demonstrates that the E. Coli AB2847 is unable to utilize DAHP, and accumulates DAHP in the medium if DAHP synthase is overexpressed. This strain was used as a host for detecting the flux committed to the aromatic pathways. Since Draths et al. (Draths, K. M., D. L. Pompliano, D. L. Conley, J. W. Frost, A. Berry, G. L. Disbrow, R. J. Staversky, and J. C. Lievens, "Biocatalytic synthesis of aromatics from D-glucose: The role of transketolase," J. Am. Chem. Soc., 1992, 114, 3956-3962) have shown a possible limitation in the production of DAHP by E4P, pATI (containing both aroG.sup.fbr and tktA) was transformed into AB2847 to eliminate the limitation of E4P. To test whether PEP supply limits DAHP production, PEP synthase (Pps) was overexpressed in AB2847/pAT1 by transforming plasmid pPS341 into this strain. 20-70 copies of the pps gene were expressed in the host cells. As a control, pPS341 was substituted by pPS341.times.1, which encodes an inactive, but stable

pps gene product. The use of the inactive Pps control allowed discrimination between the effect of Pps activity and that of protein overexpression.

Detailed Description Text - DETX (97):

As shown above, Pps overexpression improved DAHP production from glucose. We were interested to know whether the basal level of Pps expression in glucose medium contributed to the production of DAHP. Therefore, the chromosomal pps gene in strain AB2847 was knocked out. The resulting strain (JCL1362) was used as the host to repeat the above experiments. Results show that inactivation of chromosomal pps did not significantly affect the DAHP production in strains containing pRW5 or pAT1 (FIG. 2B). Therefore, the basal level of pps expression in glucose medium did not contribute to the DAHP production.

Detailed Description Text - DETX (102):

To produce tryptophan, strain ATCC31743 which contains chromosomal markers such as trpR .DELTA.(trpAE) tna can be used as a host. This strain also contains a plasmid pSC102trp which harbors trpAE operon. Plasmids pAT1 and pPS341 (or pPS706 or pPSL706) can be transformed into this strain. The serA gene can be cloned into any of the plasmids. Alternatively, these cloned genes (trpAE, aroG, tkt, pps or serA) can be consolidated to one or two plasmids. The resulting strain was grown in MT medium which contains, per liter: KH.sub.2 PO.sub.4, 3 g; K.sub.2 HPO.sub.4, 3g; K.sub.2 HPO.sub.4, 7 g; NH.sub.4 CL, 3 g; MgSO.sub.4, 0.2 g; FeSO.sub.4 7H.sub.2 O), 10 mg, glucose, 0 to 30 g.

Detailed Description Text - DETX (116):

Quinoid organics can be derived fromr dehydroquinone which is a down-stream metabolite of DAHP. To produce quinic acid, E. coli AB2848 aroD harboring pTW8090A which contains the gene qad (quinic acid dehydrogenase from Klebsiella pneumoniae) (ref: Draths, Ward, and Frost, 1992, JACS, 114, 9725-9726), and pKD136 (ref: same as above) which contains tkt, aroF, and aroB genes can be used as a host. The pps gene can be cloned into one of these plasmids and be simultaneously overexpressed. It has been reported that at least 80 mM of D-glucose can be converted into 25 mM of quinic acid. After cell removal, quinic acid in the supernatant can be converted into benzoquinone after addition of sulfuric acid and technical grade manganese (IV) dioxide and heating at 100.degree. C. for 1 h. In the absence of acidification, aqueous solutions of purified quinic acid were converted. to hydroquinone in 10% yield upon heating at 100.degree. C. for 18 h with technical grade manganese dioxide.

Claims Text - CLTX (7):

7. A process for the production of DAHP which comprises cultivating a microorganism in a nutrient medium and overexpressing the Pps gene.

Claims Text - CLTX (8):

8. The process of claim 7 wherein the step of overexpressing the Pps gene comprises transforming a plasmid selected from the group consisting of pPS341, pPSL706, and pPS706 into the microorganism.

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	6	glnap\$8	USPAT; US-PGPUB	2003/06/17 14:01
2	L2	331546	acetyl adj phosphate or acetylphosphate or acetate	USPAT; US-PGPUB	2003/06/17 14:02
3	L3	76345	promoter\$1	USPAT; US-PGPUB	2003/06/17 14:02
4	L4	1383639	induc\$8 or regulat\$8 or activat\$8 or modulat\$8	USPAT; US-PGPUB	2003/06/17 14:02
5	L5	60	2 near10 4 near10 3	USPAT; US-PGPUB	2003/06/17 14:03
6	L6	9302	pps or phosphoenol adj pyruvate adj synthase\$1	USPAT; US-PGPUB	2003/06/17 14:29
7	L7	94	6 near4 (gene\$1 or sequence\$1)	USPAT; US-PGPUB	2003/06/17 14:29
8	L8	22	7 same (overexpress\$ or amplif\$10 or increas\$8)	USPAT; US-PGPUB	2003/06/17 14:30
9	L9	17	7 and 2	USPAT; US-PGPUB	2003/06/17 14:48
10	L10	6285	lycopene\$1 or isoprenoid\$1 or carotene\$1 or astaxanthin\$1	USPAT; US-PGPUB	2003/06/17 14:58
11	L11	1	6 same 10	USPAT; US-PGPUB	2003/06/17 14:58

US-PAT-NO: 6194457

DOCUMENT-IDENTIFIER: US 6194457 B1

\*\*See image for Certificate of Correction\*\*

TITLE: Liquid eye drop composition

DATE-ISSUED: February 27, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Braswell; A. Glenn	Marine del Rey	GA	90292	N/A
Absher; Kenneth J.	Carson City	NV	89703	N/A
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APPL-NO: 09/ 015755

DATE FILED: January 29, 1998

PARENT-CASE:

This nonprovisional application claims the benefit of U.S. Provisional Application No. 06/036,516, filed Jan. 29, 1997.

US-CL-CURRENT: 514/547, 514/561, 514/562, 514/912

ABSTRACT:

A composition that is used as an eye treatment contains reduced glutathione, vitamin A and vitamin E, as well as one or more of zinc sulfate, boric acid and potassium as buffering agents. The composition also may contain a lubricant and a preservative. The composition is a sterile isotonic solution. The composition is used in a method of treating eyes for the alleviation of irritations and/or dryness, as well as for the prevention and treatment of cataracts.

20 Claims, 0 Drawing figures

Exemplary Claim Number: 1

----- KWIC -----

Brief Summary Text - BSTX (8):

Accordingly, the lens of the eye has an antioxidant defense system to respond to an oxidative stress and maintain the integrity of the lens. Various studies have shown that the antioxidant defense system includes the enzymes glutathione peroxidase, catalase and superoxide dismutase, and the antioxidants vitamin A (ascorbic acid), vitamin E (.alpha.-tocopherol) and .beta.-carotene.

See, for example, Kamei, "Glutathione Levels of the Human Crystalline Lens in Aging", *Biol. Pharm. Bull.*, vol. 16, no. 9, pps. 870-875 (1993); Fletcher et al., "Glutathione and Aging: Ideas and Evidence", *The Lancet*, vol. 344, pps. 1379-1380 (1994); and Jacques et al., "Antioxidant Status in Persons With and Without Senile Cataracts", *Arch. Ophthalmol.*, vol. 106, pps. 337-340 (1988).

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	6	glnap\$8	USPAT; US-PGPUB	2003/06/17 14:01
2	L2	331546	acetyl adj phosphate or acetylphosphate or acetate	USPAT; US-PGPUB	2003/06/17 14:02
3	L3	76345	promoter\$1	USPAT; US-PGPUB	2003/06/17 14:02
4	L4	1383639	induc\$8 or regulat\$8 or activat\$8 or modulat\$8	USPAT; US-PGPUB	2003/06/17 14:02
5	L5	60	2 near10 4 near10 3	USPAT; US-PGPUB	2003/06/17 14:03
6	L6	9302	pps or phosphoenol adj pyruvate adj synthase\$1	USPAT; US-PGPUB	2003/06/17 14:29
7	L7	94	6 near4 (gene\$1 or sequence\$1)	USPAT; US-PGPUB	2003/06/17 14:29
8	L8	22	7 same (overexpress\$ or amplif\$10 or increas\$8)	USPAT; US-PGPUB	2003/06/17 14:30
9	L9	17	7 and 2	USPAT; US-PGPUB	2003/06/17 14:48
10	L10	6285	lycopene\$1 or isoprenoid\$1 or carotene\$1 or astaxanthin\$1	USPAT; US-PGPUB	2003/06/17 14:58
11	L11	1	6 same 10	USPAT; US-PGPUB	2003/06/17 14:58
12	L12	1563	6 and 2	USPAT; US-PGPUB	2003/06/17 15:01
13	L13	1563	12 and 6	USPAT; US-PGPUB	2003/06/17 15:01
14	L14	3593	10 and 2	USPAT; US-PGPUB	2003/06/17 15:01
15	L15	9	14 and 6	USPAT; US-PGPUB	2003/06/17 15:01



PGPUB-DOCUMENT-NUMBER: 20030036518

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030036518 A1

TITLE: ARTIFICIAL POLYMERIC MEMBRANE STRUCTURE, METHOD FOR  
PREPARING SAME, METHOD FOR PREPARING THIS POLYMER,  
PARTICLE AND FILM CONTAINING THIS STRUCTURE

PUBLICATION-DATE: February 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
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PEROCHON, ETIENNE	TOULOUSE		FR	

APPL-NO: 09/ 284754

DATE FILED: April 20, 1999

CONTINUED PROSECUTION APPLICATION: This is a publication of a continued prosecution application (CPA) filed under 37 CFR 1.53(d).

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
FR	9613101	1996FR-9613101	October 23, 1996

PCT-DATA:

APPL-NO: PCT/FR97/01891

DATE-FILED: Oct 22, 1997

PUB-NO:

PUB-DATE:

371-DATE:

102(E)-DATE:

US-CL-CURRENT: 514/44, 424/443 , 424/490

ABSTRACT:

The invention concerns an artificial membranous structure analogous to fixed plasmic membranes which comprise a solid substrate (61); a functional membrane (63) which does not circumscribe the external medium; and at least one bifunctional fixing compound (62) inserted between the membrane (63) and the substrate (61), cooperating by polyelectrolytic complexing with the substrate (61) and by lyotropic bonds with the membrane (63). The invention also concerns the use of this structure for obtaining a medicament, a particle, a film, its method of preparation, as well as a lipidic polycationic polymer, and a method for its preparation, acting as a bifunctional compound (62).

----- KWIC -----

Summary of Invention Paragraph - BSTX (40):

[0040] Advantageously and according to the invention, the membranous ligands are selected from among phospholipids, fatty acids, isoprenoids, peptides, fatty amines, ethers, sterols, terpenes, glycolipids, shingolipids, gangliosides and ceramides.

Detail Description Paragraph - DETX (54):

[0152] Preparation of viral particles with a membrane containing DPPE 3-mercaptopropionate. 12 mg of particles containing 10 mg of phospholipids and 200 .mu.g of DPPE (0.26 .mu.mol) were dispersed in 30 ml of a 75 mM sodium acetate buffer brought to pH 8.5 by adding a bicarbonate buffer. 100 .mu.l of a 15 mM solution of succinimidyl 3-(2-pyridyldithio) propionate (SDDP) were added and vigorous stirring was carried out for 1 h. 6 ml of a 1M sodium acetate solution were then added. The suspension was then dialysed against a 20 mM sodium acetate buffer. 2.3 mg (15 .mu.mol) of dithiothreitol in a sodium carbonate buffer were added and the suspension was kept under argon at pH 7.5 for 1 h. The pH was then adjusted to 5.2 by adding a sodium acetate buffer and the suspension was then dialysed against a 20 mM sodium acetate buffer. A preparation was obtained containing 0.1 .mu.mol of DPPE modified by mercaptopropionate.

Detail Description Paragraph - DETX (58):

[0156] 1 .mu.mol of modified transferrin dissolved in a 100 mM, pH 7.8, phosphate buffer was mixed with particles containing 0.1 .mu.mol of DPPE 3-mercaptopropionate and dispersed in a 20 mM sodium acetate buffer. The preparation was stirred for 24 hours at room temperature and was then subjected to ultrafiltration through a 100 KD membrane to remove excess transferrin.

Detail Description Paragraph - DETX (99):

[0187] The particles were dispersed in 150 ml of a 150 mM PPS buffer, of pH 7.1, and gently stirred. Aliquots were withdrawn at regular intervals of time and the concentration of doxorubicin present in the supernatant was measured by/spectrophotometry at 480 nm.

Claims Text - CLTX (7):

7. The membranous structure as claimed in one of claims 1 to 6, wherein the membranous ligands (65, 66) are selected from phospholipids, fatty acids, isoprenoids and peptides.

PGPUB-DOCUMENT-NUMBER: 20020094977

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020094977 A1

TITLE: HMG-CoA reductase inhibitors and method

PUBLICATION-DATE: July 18, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
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APPL-NO: 10/ 007407

DATE FILED: December 4, 2001

RELATED-US-APPL-DATA:

child 10007407 A1 20011204

parent continuation-in-part-of 09875155 20010606 US PENDING

non-provisional-of-provisional 60211595 20000615 US

US-CL-CURRENT: 514/215, 514/291 , 540/586 , 546/80

ABSTRACT:

Compounds of the following structure are HMG CoA reductase inhibitors and thus are active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and atherosclerosis 1

and pharmaceutically acceptable salts thereof, wherein X is O, S, SO, SO.sub.2 or NR.sub.7;

Z is 2

n is 0 or 1;

R.sub.1 and R.sub.2 are the same or different and are independently selected from alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroalkyl; and

R.sub.3 to R.sub.10 are as defined herein.

[0001] This application is a continuation-in-part of U.S. application Ser. No. 09/875,155 filed Jun. 6, 2001 which application claims priority from U.S. provisional application No. 60/211,595, filed Jun. 15, 2000.

----- KWIC -----

Summary of Invention Paragraph - BSTX (195):

[0192] The squalene synthetase inhibitors suitable for use herein include, but are not limited to, .alpha.-phosphono-sulfonates disclosed in U.S. Pat. No. 5,712,396, those disclosed by Biller et al, J. Med. Chem., 1988, Vol. 31, No. 10, pp 1869-1871, including isoprenoid (phosphinylmethyl)phosphonates as well as other known squalene synthetase inhibitors, for example, as disclosed in U.S. Pat. No. 4,871,721 and 4,924,024 and in Biller, S. A., Neuenschwander, K., Ponpipom, M. M., and Poulter, C. D., Current Pharmaceutical Design, 2, 1-40 (1996).

Summary of Invention Paragraph - BSTX (210):

[0207] an anti-oxidant such as beta-carotene, ascorbic acid, .alpha.-tocopherol or retinol as disclosed in WO 94/15592 as well as Vitamin C and an antihomocysteine agent such as folic acid, a folate, Vitamin B6, Vitamin B12 and Vitamin E;

Summary of Invention Paragraph - BSTX (290):

[0287] a chondroprotective compound such as a polysulfated glycosaminoglycan (PSGAG), glucosamine, chondroitin sulfate (CS), hyaluronic acid (HA), pentosan polysulfate (PPS), doxycycline or minocycline, such as disclosed in EP 970694;

Detail Description Paragraph - DETX (9):

[0370] A mixture of crude Part B compound (17.0 g, 27.3 mmol), ammonium acetate (9.34 g, 120 mmol) and copper acetate monohydrate (20.54 g, 101 mmol) in glacial acetic acid (100 ml) was refluxed under argon for 19 hours. The mixture was poured into an ice-cold solution of concentrated ammonium hydroxide (85 ml) in water (170 ml) and the bright blue solution was extracted with ether (3.times.200 ml). The combined organic extracts were washed with water (2.times.80 ml) and brine (80 ml), dried (anhydrous Na.sub.2SO.sub.4), filtered, evaporated to dryness, and dried in vacuo. The crude product (14 g, brown syrup) was chromatographed in two batches, each on a silica gel column (EM, 2-1/4".times.10") to give the desired product as an off-white solid (4.161 g). An additional 931 mg of product was obtained from chromatography of mixed fractions. Yield: 5.092 g, 46% from compound A). Rf 0.53 (Silica gel; EtOAc:Hexane-1:4; UV) 41

Detail Description Paragraph - DETX (10):

[0371] A solution of Part C compound (2.515 g, 6.23 mmol) in dry THF (30 ml) was cooled to 0.degree. C. (ice-water bath), treated dropwise with lithium aluminum hydride (1.0 M in THF; 12.5 ml, 12.5 mmol), stirred at 0.degree. C. for 30 minutes then at room temperature for 3 hours. The reaction mixture was cooled to 0.degree. C., treated successively with water (0.5 ml), 15% NaOH (0.5 ml) and water (1.5 ml), stirred at room temperature for 5 minutes then diluted with ethyl acetate (50 ml). The slurry was filtered through a Celite.RTM. pad, washing the pad well with ethyl acetate (3.times.25 ml). The clear filtrate was evaporated to dryness and dried in vacuo to give the title

product. Yield: 2.386 g, white foam (100 %). Rf 0.15 (Silica gel; EtOAc:Hexane-1:4; UV) 42

Detail Description Paragraph - DETX (11):

[0372] A solution of Part D compound (2.27 g, 6.23 mmol) in dry dichloromethane (45 ml) was cooled to 0.degree. C. (ice-water bath) and treated dropwise with phosphorus tribromide (1.0 M in dichloromethane; 12.5 ml, 12.5 mmol). The ice bath was removed and the reaction mixture was stirred at room temperature for 30 minutes after which it was re-cooled to 0.degree. C. and treated dropwise with saturated sodium bicarbonate (70 ml). The mixture was then warmed to room temperature and extracted with ethyl acetate (2.times.100 ml). The combined organic extracts were washed with water (2.times.50 ml) and brine (50 ml), re-extracting each aqueous wash with dichloromethane (100 ml). The organic extracts were dried (anhydrous sodium sulfate), filtered, evaporated to dryness and dried in vacuo to give the title product as a white solid. Yield: 2.503 g, (94%). m.p.=169-171.degree. C. Rf 0.58 (Silica gel; EtOAc:Hexane- 1:4; UV). 43

Detail Description Paragraph - DETX (12):

[0373] A solution of diethyl phosphite (0.88 ml, 6.83 mmoles) in dry THF (10 ml) was cooled to -10.degree. C. (acetonitrile-dry ice bath), treated with sodium (bistrimethylsilyl)amide (1.0 M in THF; 6.7 ml, 6.7 mmol) and stirred at -10.degree. C. for 30 minutes. The cooled solution was treated with a solution of Part E compound (2.41 g, 5.68 mmol) in dry THF (20 ml), stirred at -10.degree. C. for 1.0 hour then quenched at -10.degree. C. with water (14 ml). The solution was extracted with ethyl acetate (2.times.75 ml) and the combined organic extracts washed with 1.0 M hydrochloric acid (8.0 ml) and brine (10 ml), dried (anhydrous sodium sulfate), filtered, evaporated to dryness and dried in vacuo. The crude product (3.12 g, syrup) was chromatographed on a silica gel column (EM, 5.5 cm.times.12.5 cm) to give the title compound as a syrup. Yield: 2.34 g (85.5%). Rf 0.33 (Silica gel; EtOAc:Hexane-1:1; UV). 44

Detail Description Paragraph - DETX (13):

[0374] A solution of Part F compound (2.29 g, 4.756 mmol) in dry THF (20 ml) was cooled to -78.degree. C., treated with 2.37 M n-butyllitium (2.41 ml, 5.71 mmol) and stirred at -78.degree. C. for 40 minutes. The solution was treated dropwise via cannula with a -78.degree. C. solution of Part A(I) compound (2.36 g, 9.15 mmol) in dry THF (10 ml), keeping both solutions at -78.degree. C. at all times. The reaction mixture was stirred at -78.degree. C. for 1.0 hr, -10.degree. C. for 1.0 hr and at room temperature for 5 hr, quenched with 25% ammonium chloride solution (12 ml) then extracted with ethyl acetate (2.times.100 ml). The combined organic extracts were washed with 25% ammonium chloride solution (12 ml) and brine (12 ml), dried (anhydrous sodium sulfate), filtered, evaporated to dryness and dried in vacuo. The crude product yellow syrup was chromatographed on a silica gel column (EM, 2-1/4".times.10") to afford the title compound as a syrup. Yield: 878 mg (32%). Rf 0.37 (Silica gel; EtOAc:Hexane-1:4; UV). 45

Detail Description Paragraph - DETX (14):

[0375] A solution of Part G compound (850 mg, 1.45 mmol) in dry dichloromethane (20 ml) was cooled to 0.degree. C., treated with trifluoroacetic acid (1.85 ml, 24 mmol), stirred at 0.degree. C. for 5 minutes, then at room temperature for 4.5 hours. The reaction mixture was poured slowly into a 1 L flask containing ethyl acetate (300 ml) and saturated sodium bicarbonate (40 ml), rinsing the flask with ethyl acetate (50 ml). The mixture was stirred well and the phases separated, washing the organic phase with saturated sodium bicarbonate (25 ml) and brine (25 ml). The organic phase was dried over anhydrous sodium sulfate, filtered, evaporated to dryness and dried in vacuo. The crude product mixture was chromatographed on a silica gel column (EM, 1.5".times.12") to give the desired compound as a syrup. Yield: 570 mg (83%). Rf 0.23 (Silica gel; EtOAc:Hexane-1:1; UV) 46

Detail Description Paragraph - DETX (64):

[0419] (prepared as described in Example 2 Parts A, B and C except methyl isobutyryl acetate is substituted for ethyl isobutyryl acetate) and toluene (170 mL). The mixture is stirred at 20-25.degree. C. until a clear solution is obtained. A solution of 65% Red-Al in toluene (57.8 mL, 192.6 mmol) is added and the reaction mixture is heated to 80.degree. C. until complete as determined by HPLC. The reaction mixture is cooled to 20.degree. C. and quenched by pouring it into cold (0-5.degree. C.) 20% HCl (495 mL). Phases are separated and the spent toluene phase is discarded. The pH of the aqueous phase is adjusted from <0 to 4-5 with 10N NaOH. Ethyl acetate (500 mL) is added and the pH adjustment continued to 7-8. The phases are separated. The aqueous phase is extracted with additional ethyl acetate (2.times.500 mL). The combined rich ethyl acetate solution is washed with water (3.times.250 mL) and concentrated under reduced pressure to .about.465 mL. This solution is carried through to the next oxidation step.

Detail Description Paragraph - DETX (65):

[0420] The rich ethyl acetate solution is charged from above into a three neck 1-L flask equipped with mechanical stirring, temperature controller, and addition funnel and cooled to 0-5.degree. C. To the slurry, potassium bromide (1.53 g, 12.8 mmol) and TEMPO (2,2,6,6-tetramethyl-1-piperidinylo-xy) (0.20 g, 1.28 mmol) are added. The pH of NaOCl (sodium hypochlorite) solution (212.1 mL) is adjusted to .about.9.1 and added to the slurry at a rate such that the temperature remained at 0-5.degree. C. Stirring is continued at 0-5.degree. C. until the reaction is complete as determined by HPLC. The aqueous phase is extracted with EtOAc (2.times.200 mL). The combined rich organic phase is washed with a 1:1 solution of sat. aq. Na.sub.2S.sub.2O.sub.3 (sodium thiosulfate) (75 mL) and water (75 mL) followed by wash of the rich organic phase with 1N NaOH (250 mL). The rich organic phase is washed with water (250 mL) and concentrated to .about.100 mL under reduced pressure. Isopropanol (IPA) (400 mL) is added and the resulting mixture is heated to reflux (80-85.degree. C.). The solution is distilled to a volume of .about.250 mL. Water (50 mL) is added and the crystal slurry is stirred at 70-80.degree. C. for 1 h then allowed to cool to 20-25.degree. C. over at least 1 h. The slurry is held at 20-25.degree. C. for at least 1 h before collecting the solid by filtration on a Buchner funnel. The cake is washed with cold (0.degree. C.) IPA/water (4:1) (2.times.50 mL) and dried to a constant weight under vacuum at

40.degree. C. to afford title aldehyde.

Detail Description Paragraph - DETX (77):

[0428] An N.sub.2 purged 250 mL 3-neck rb flask is charged with Example 27 pyridine derivative (18) (5 g, 13.9 mmol), Example 28 sulfone (16) (6.9 g, 15.3 mmol) and THF (75 mL). The stirred solution is cooled to -74 to -78.degree. C. Slowly a 1M solution of LiHMDS (lithium bis(trimethylsilyl)amide) (15.3 mL, 15.3 mmol) in THF is charged at a rate such that the temperture remained between -70 and -78.degree. C. After addition of the base is complete, the reaciton mixture is warmed to .about.-45.degree. C. over .about.15 minutes. The stirred reaction is quenched at -70.degree. C. by slow addition of sat. aq. NH.sub.4Cl (7.5 mL) solution and water (38 mL). The dry ice bath is removed and the solution is warmed to 20-25.degree. C. from the reaction mixture. Ethyl acetate (50 mL) is added, the mixture agitated, and layers separated. The organic layer is washed with saturated sodium bicarbonate solution (2.times.38 mL) followed by brine (25 mL) and concentrated to a volume of 50 mL. Acetonitrile (50 mL) is added and the solution is concentrated to a volume of 50 mL. This step is repeated. Water (.about.5-6 mL) is slowly added to the hot solution (60-70.degree. C.) until the cloud point is reached. The thin slurry is held for 30 min at high temperature and then slowly cooled over several hours with stirring. The product is filtered, cake is washed with a 5:1 mixture of acetonitrile and water, and dried to afford the title compound.

Claims Text - CLTX (41):

40. The combination as defined in claim 21 wherein the other therapeutic agent is an anti-Alzheimer's agent or anti-dementia agent, which is tacrine HCl (Cognex.RTM.), donepezil (Aricept.RTM.), a .gamma.-secretase inhibitor, a .beta.-secretase inhibitor and/or antihypertensive agent; an antiosteoporosis agent, which is parathyroid hormone, a bisphosphonate, alendronate, a Ca receptor agonist or a progestin receptor agonist; a hormone replacement therapeutic agent, which is a selective estrogen receptor modulator (SERM); a tyrosine kinase inhibitor; a selective androgen receptor modulator; an antiarrhythmic agent, which is a .beta.-blocker, or a calcium channel blocker, or an .alpha.-adrenergic blocker; coenzyme Q sub. 10; an agent that upregulates type III endothelial cell nitric acid syntase; a chondroprotective compound which is polysulfated glycosaminoglycan (PSGAG), glucosamine, chondroitin sulfate (CS), hyaluronic acid (HA), pentosan polysulfate (**PPS**), doxycycline or minocycline; a cyclooxygenase (COX)-2 inhibitor, which is Celebrex.RTM. (Searle) or Vioxx.RTM. (Merck) or a glycoprotein IIa/IIIb receptor antagonist; a 5-HT reuptake inhibitor; a growth hormone secretagogue; an anti-atherosclerosis agent; an anti-infective agent, or an immunosuppressant for use in transplantation, or an antineoplastic agent.

PGPUB-DOCUMENT-NUMBER: 20020061901

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020061901 A1

TITLE: HMG-CoA reductase inhibitors and method

PUBLICATION-DATE: May 23, 2002

INVENTOR-INFORMATION:

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APPL-NO: 10/ 008154

DATE FILED: December 4, 2001

RELATED-US-APPL-DATA:

child 10008154 A1 20011204

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non-provisional-of-provisional 60211594 20000615 US

US-CL-CURRENT: 514/290, 514/278 , 546/15 , 546/79 , 546/93

ABSTRACT:

Compounds of the following structure are HMG CoA reductase inhibitors and thus are active in inhibiting cholesterol biosynthesis, modulating blood serum lipids, for example, lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, dyslipidemia, hormone replacement therapy, hypercholesterolemia, hypertriglyceridemia and atherosclerosis as well as Alzheimer's disease and osteoporosis 1

and pharmaceutically acceptable salts thereof, 2

n is 0 or 1;

x is 0, 1, 2, 3 or 4;

y is 0, 1, 2, 3 or 4, provided that at least one of x and y is other than 0;

and optionally one or more carbons of (CH.sub.2).sub.x and/or (CH.sub.2).sub.y together with additional carbons form a 3 to 7 membered spirocyclic ring;

R.sub.1 and R.sub.2 are the same or different and are independently selected from alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroalkyl;

R.sub.3 is H or lower alkyl;

R.sub.4 and R.sub.7 are as defined herein.

[0001] This application is a continuation-in-part of U.S. application Ser.



No. 09/875,218 filed Jun. 6, 2001, which application claims priority from U.S. provisional application No. 60/211,594, filed Jun. 15, 2000.

----- KWIC -----

Summary of Invention Paragraph - BSTX (171):

[0168] Referring to Scheme 5, the arginine salt of the compounds of formula I of the invention may be prepared by treating alkali metal salt (preferably sodium) Ib with acid (TFA, HCl) to form the acid Ib.sup.6 which is treated with arginine in the presence of suitable solvents such as ethyl alcohol and H.sub.2O, ethyl acetate, acetonitrile and the like, to form arginine salt Ib.sup.7. 31

Summary of Invention Paragraph - BSTX (192):

[0189] The squalene synthetase inhibitors suitable for use herein include, but are not limited to, .alpha.-phosphono-sulfonates disclosed in U.S. Pat. No. 5,712,396, those disclosed by Biller et al, J. Med. Chem., 1988, Vol. 31, No. 10, pp 1869-1871, including isoprenoid (phosphinyl-methyl)phosphonates as well as other known squalene synthetase inhibitors, for example, as disclosed in U.S. Pat. Nos. 4,871,721 and 4,924,024 and in Biller, S. A., Neuenschwander, K., Ponpipom, M. M., and Poulter, C. D., Current Pharmaceutical Design, 2, 1-40 (1996).

Summary of Invention Paragraph - BSTX (207):

[0204] an anti-oxidant such as beta-carotene, ascorbic acid, .alpha.-tocopherol or retinol as disclosed in WO 94/15592 as well as Vitamin C and an antihomocysteine agent such as folic acid, a folate, Vitamin B6, Vitamin B12 and Vitamin E;

Summary of Invention Paragraph - BSTX (287):

[0284] a chondroprotective compound such as a polysulfated glycosaminoglycan (PSGAG), glucosamine, chondroitin sulfate (CS), hyaluronic acid (HA), pentosan polysulfate (PPS), doxycycline or minocycline, such as disclosed in EP 970694;

Detail Description Paragraph - DETX (6):

[0362] To a stirred solution of crude Part C compound (26.9 mmol) in HOAc (128 mL) was added ammonium acetate (9.14 g, 118.6 mmol) and copper (II) acetate monohydrate (19.7 g, 99.7 mmol). The reaction mixture was heated at reflux under argon overnight. After cooling to room temperature, the reaction mixture was poured into a mixture of NH.sub.4OH (150 mL) and ice (.sup. about 300 g), then extracted with Et.sub.2O (3.times. 100 mL). The combined Et.sub.2O extracts were washed with H.sub.2O and brine, then dried (Na.sub.2SO.sub.4), filtered and concentrated in vacuo. Purification by flash chromatography (2:20:80-EtOAc/CH.sub.2Cl.sub.2/hexane) gave the title compound as a white foam, 7.7 g, 71% yield (from Part B compound). 41

Detail Description Paragraph - DETX (17):

[0371] A 1 L 3-necked round bottom flask was flame-dried and then fitted with a mechanical stirrer, an argon-filled balloon, vacuum take-off and a thermocouple. To a stirred slurry of Part (1) compound (7.00 g, 12.9 mmol) in THF (200 mL) at 0.degree. C. was added n-butyllithium solution (5.4 mL, 2.5 M in hexanes, 13.5 mmol) over 20 min. A deep red-orange solution formed. After 30 min, a solution of zinc chloride-N,N,N',N'-tetraamethylethylene-diamine complex (dried in vacuo at 60.degree. C. for 2 h, 2.42 g, 13.5 mmol) in THF (100 mL) was added via cannula and stirred 30 min. After 30 min, the resulting solution was cannulated into a solution of Example 2 Part G aldehyde (4.30 g, 16.6 mmol) in THF (20 mL) at room temperature over 20 min. A light orange solution soon formed, followed by a precipitate. After 3 h, the reaction was quenched with brine (50 mL) and water (50 mL) and extracted three times with ethyl acetate (100 mL). The organic extracts were combined, dried (MgSO<sub>4</sub>) and evaporated. LCMS of the crude material indicated unreacted Part (1) compound and an 89/11 mixture of the desired (E) isomer/undesired (Z) isomer.

Detail Description Paragraph - DETX (21):

[0374] To a solution of 4-fluoro-benzaldehyde (5 g, 40.3 mmol) and ethyl isobutyryl acetate (6.5 mL, 40.3 mmol) in benzene (50 mL) was added piperidine (400 .mu.L, 4.04 mmol), followed by acetic acid (100 .mu.L, 1.66 mmol). The reaction was refluxed for 16 hours and partitioned between aqueous HCl (1N, 20 mL) and ethyl acetate (50 mL .times.2). The combined organic layers were washed with saturated NaHCO<sub>3</sub> (20 mL), brine (10 mL), and dried over sodium sulfate (Na<sub>2</sub>SO<sub>4</sub>). The solvent was removed in vacuo. Distillation at 140.degree. C. at 300 mm Hg afford 9.06 g (85% yield) of compound A as a yellow oil. ESI-LC/MS (M+H)<sup>+</sup>=264. 50

Detail Description Paragraph - DETX (23):

[0376] To a solution of the crude compound B (12 g) in aqueous HOAc (100 mL) was added ammonium acetate (9.5 g, 123.2 mmol), followed by cupric acetate monohydrate (20.7 g, 113.9 mmol). The reaction was reflux for 20 hours, cooled to room temperature, then poured into a solution of ammonium hydroxide in ice (1 to 1; v/v). The aqueous layer was extracted with ethyl ether (200 mL.times.3). The combined organic layers were washed with water (50 mL) and brine (50 mL). Flash chromatography (10% ethyl acetate in hexane) afforded 10.2 g (88% yield) of compound C as white powder. ESI-LC/MS (M+H)<sup>+</sup>=404; m.p. 138-140.degree. C. 52

Detail Description Paragraph - DETX (24):

[0377] To a solution of compound C (10 g, 24.78 mmol) in anhydrous THF (240 mL) at 0.degree. C. was added 1.0 M lithium aluminum hydride in THF (74 mL, 74 mmol). The reaction was stirred at 0.degree. C. for 1 hour and then warmed to room temperature and stirred for 16 hours. The reaction was then cooled to 0.degree. C. and quenched slowly with ice, then sodium hydroxide (10% NaOH, 20 mL). The mixture was extracted with diethyl ether (50 mL.times.2) and filtered. The filter cake was then washed with more ethyl ether (10 mL) and ethyl acetate (10 mL). The combined organic layers were washed with water (10 mL) and brine (10 mL), then dried over sodium sulfate (Na<sub>2</sub>SO<sub>4</sub>). Flash chromatography (20% ethyl acetate in hexane) afforded 6.5 g (73% yield)

of compound D. ESI-LC/MS (M+H).sup.+ = 362; m.p. 170-171.degree. C. 53

Detail Description Paragraph - DETX (25):

[0378] To a solution of compound D (8.5 g, 23.54 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (100 mL) at 0.degree. C. was slowly added 1.0 M phosphorous tribromide in CH<sub>2</sub>Cl<sub>2</sub> (47 mL, 47.1 mmol) while maintaining the temperature below 10.degree. C. After the addition was complete, the reaction was stirred at 0.degree. C. for 1 hour and then poured into saturated cold NaHCO<sub>3</sub> solution (200 mL) with stirring. The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (50 mL.times.2) and the combined organic layer was washed with water (10 mL) and brine (10 mL), then dried over sodium sulfate (Na<sub>2</sub>SO<sub>4</sub>). Flash chromatography (10% ethyl acetate in hexane) gave 8.6 g (86% yield) of compound E as a white solid. ESI-LC/MS (M+H).sup.+ = 424; m.p. 157-159.degree. C. 54

Detail Description Paragraph - DETX (26):

[0379] To a solution of diethyl phosphite (785 .mu.L, 6.09 mmol) in anhydrous THF (25 mL) at -10.degree. C. under argon was added a 1.0 M THF solution of sodium hexamethyldisazide (6 mL, 6.09 mmol). The reaction mixture was stirred at -10.degree. C. for 30 minutes. A solution of compound E (2.15 g, 5.08 mmol) in THF was added to the reaction while maintaining the temperature at -10.degree. C. After the addition was complete, the reaction was stirred for 1 hour and quenched with water (20 mL). The aqueous layer was extracted with ethyl acetate (30 mL.times.2) and the combined organic layers were washed with 1N HCl solution (5 mL). The organic solvent was removed in vacuo. Flash chromatography using 20% to 30% ethyl acetate in hexane as eluting afforded 2.29 g (94% yield) of compound F as a white solid. ESI-LC/MS (M+H).sup.+ = 482; m.p. 102-105.degree. C. 55

Detail Description Paragraph - DETX (29):

[0382] To a cooled (-78.degree. C.) solution of compound F (2.02 g, 4.19 mmol) in anhydrous THF (30 mL) under argon was slowly added a 2.5 M THF solution of n-butyllithium (2.1 mL) over a period of 40 minutes. The temperature was maintained below -75.degree. C. during the addition. After the addition was complete, the reaction mixture was stirred for another 40 minutes at -78.degree. C. A solution of compound G (2.2 g, 8.52 mmol) in THF under argon was cannulated into the phosphonate mixture at -78.degree. C. After the addition was complete, the reaction was stirred for 1 hour at -78.degree. C. The reaction was then warmed to -10.degree. C. and stirred for 1 hour and then stirred at room temperature for an additional hour. The mixture was quenched with saturated ammonium chloride solution (5 mL) and extracted with ethyl acetate (60 mL.times.3). The combined organic layers were washed with water (10 mL) and brine (10 mL), then dried over sodium sulfate (Na<sub>2</sub>SO<sub>4</sub>) and filtered. The filtrate was concentrated in vacuo. Flash chromatography using 5% to 10% ethyl acetate in hexane as eluent afforded 1.48 g (60% yield) of compound H as a white solid. ESI-LC/MS (M+H).sup.+ = 586; m.p. 148-149.degree. C. 57

Detail Description Paragraph - DETX (30):

[0383] To a cooled (0.degree. C.) solution of compound H (500 mg, 0.854 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (12 mL) under argon was slowly added trifluoroacetic acid (987 mL, 12.82 mmol). After the addition was complete, the reaction mixture was allowed to stirred at 0.degree. C. for 10 minutes and at room temperature for 3 hours and then the solvent was removed in vacuo. The reaction mixture was quenched with phosphate solution (pH 7.5, 12 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (20 mL.times.2). The combined organic layers were washed with brine (10 mL), dried over sodium sulfate (Na<sub>2</sub>SO<sub>4</sub>), and filtered. The solvent was removed in vacuo. Flash silica gel chromatography using 30% to 50% ethyl acetate in hexane as an eluent afforded 331 mg (80% yield) of compound I as a white powder. ESI-LC/MS (M+H).sup.+ = 588; m.p. = 199-200.degree. C. 58

Detail Description Paragraph - DETX (38):

[0389] To part H(1) compound (109 mg, 0.2 mmol) in 25 mL 2-necked round bottom flask (flame-dried and fitted with an argon-filled balloon, vacuum take-off and a thermocouple) was added 0.5 mL of DMPU (distilled over CaH<sub>2</sub> under reduced pressure, stored with 4A molecular sieves). The resulting slurry was warmed while stirring until becoming a clear solution, which was diluted with THF (1.5 mL). The reaction mixture was evacuated and purged three times with argon, then cooled to -78.degree. C. To the cooled reaction mixture was added dropwise 0.42 mL of a 0.5 M solution of LDA in THF<sub>sup.1</sub> (0.21 mmol). An amber colored solution formed. After stirring at -78.degree. C. for 30 minutes, a solution of Example 2 Part G aldehyde (67 mg, 0.26 mmol) in THF (0.5 mL) was added via a syringe. After addition, the resulting yellow solution was stirred at -78.degree. C. for 30 minutes, then at 0.degree. C. for 1 hour before quenched with an aqueous solution of ammonium chloride. The reaction mixture was extracted three times with ethyl acetate (10 mL). The organic extracts were combined, washed with water and brine, dried (MgSO<sub>4</sub>) and evaporated. The crude product was purified using flash chromatography on silica gel eluting with 5% EtOAc/hexane. The desired fractions were pooled and concentrated, and the collected residue dried in vacuo overnight to give Part H(2) compound as a white foam, 80 mg (68% yield).

Detail Description Paragraph - DETX (43):

[0393] To a cooled (0.degree. C.) solution of Part A compound (450 mg, 0.766 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (9 mL) under argon was slowly added trifluoroacetic acid (886 mL, 12.5 mmol). After the addition was complete, the reaction mixture was allowed to stirred at 0.degree. C. for 10 minutes and at room temperature for 3 hours and then the solvent was removed in vacuo. The reaction mixture was quenched with phosphate solution (pH 7.5, 12 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (20 mL.times.2). The combined organic layer was washed with brine (saturated NaCl solution, 10 mL), dried over sodium sulfate (Na<sub>2</sub>SO<sub>4</sub>) and filtered. The solvent was removed in vacuo. Flash silica gel chromatography using 30% to 50% ethyl acetate in hexane as an eluent afford 330 mg (91% yield) part B compound as a white powder. ESI-LC/MS (M+H).sup.+ = 474, MP (.degree. C.) = 253-254. 63

Detail Description Paragraph - DETX (54):

[0402] To a mixture of 4-fluoro-benzaldehyde (935.8 g, 7.54 moles) and

methyl isobutyryl acetate (1087 g, 7.54 moles) was added piperidine (64.2 g, 0.75 mol), followed by acetic acid (22.6 g, 0.38 mol). The mixture was heated to 80 to 85.degree. C. for about 2 hours. 16 Liters (4.times.4L) of toluene was added and mixed with the reaction mixture. The toluene was removed using a rotavapor (50-65.degree. C./20-90 torr), leaving a yellow oil. The yellow oil was dissolved in 5 L MTBE and washed with:

Detail Description Paragraph - DETX (60):

[0408] To a solution of the crude compound B (3078 g) in aqueous HOAc (16 L) was added ammonium acetate (1446 g), followed by cupric acetate monohydrate (1859 g). The reaction was refluxed between 120 to 124.degree. C. for 12-15 hours. Approximately 90% of the acetic acid was evaporated to produce a green slurry. The slurry was then mixed with 14 L MTBE.

Detail Description Paragraph - DETX (66):

[0414] To a 500 mL round bottom flask equipped with a magnetic stirrer and a nitrogen inlet was charged Part C compound (17) (Scheme 6) (50.0 g, 128.4 mmol) and toluene (170 mL). The mixture was stirred at 20-25.degree. C. until a clear solution was obtained. A solution of 65% Red-Al in toluene (57.8 mL, 192.6 mmol) was added and the reaction mixture was heated to 80.degree. C. until complete as determined by HPLC. The reaction mixture was cooled to .about.20.degree. C. and quenched by pouring it into cold (0-5.degree. C.) 20% HCl (495 mL). Phases were separated and the spent toluene phase was discarded. The pH of the aqueous phase was adjusted from <0 to 4-5 with 10N NaOH. Ethyl acetate (500 mL) was added and the pH adjustment continued to 7-8. The phases were separated. The aqueous phase was extracted with additional ethyl acetate (2.times.500 mL). The combined rich ethyl acetate solution was washed with water (3.times.250 mL) and concentrated under reduced pressure to .about.465 mL. This solution was carried through to the next oxidation step.

Detail Description Paragraph - DETX (67):

[0415] The rich ethyl acetate solution was charged from above into a three neck 1-L flask equipped with mechanical stirring, temperature controller, and addition funnel and cooled to 0-5.degree. C. To the slurry, potassium bromide (1.53 g, 12.8 mmol) and TEMPO (2,2,6,6-tetramethyl-1-piperidinylo-xy) (0.20 g, 1.28 mmol) were added. The pH of NaOCl (sodium hypochlorite) solution (212.1 mL) was adjusted to 9.1 and added to the slurry at a rate such that the temperature remained at 0-5.degree. C. Stirring was continued at 0-5.degree. C. until the reaction was complete as determined by HPLC. The aqueous phase was extracted with EtOAc (2.times.200 mL). The combined rich organic phase was washed with a 1:1 solution of sat. aq. Na.sub.2S.sub.2O.sub.3 (sodium thiosulfate) (75 mL) and water (75 mL) followed by wash of the rich organic phase with 1N NaOH (250 mL). The rich organic phase was washed with water (250 mL) and concentrated to .about.100 mL under reduced pressure. Isopropanol (IPA) (400 mL) was added and the resulting mixture was heated to reflux (80-85.degree. C.). The solution was distilled to a volume of .about.250 mL. Water (50 mL) was added and the crystal slurry was stirred at 70-80.degree. C. for 1 h then allowed to cool to 20-25.degree. C. over at least 1 h. The slurry was held at 20-25.degree. C. for at least 1 h before collecting the solid by filtration on a Buchner funnel. The cake was washed with cold (0.degree. C.)

IPA/water (4:1) (2.times.50 mL) and dried to a constant weight under vacuum at 40.degree. C. to afford 41.5 g (90%) of title aldehyde as a white crystalline solid.

Detail Description Paragraph - DETX (74):

[0420] A.sub.n N.sub.2 purged 250 mL 3-neck rb flask was charged with Example 35 pyridine derivative (18) (5.0 g, 13.9 mmol), Example 36 sulfone (16) (6.92 g, 15.3 mmol) and THF (75 mL). The stirred solution was cooled to -74 to -78.degree. C. Slowly a 1M solution of LHMDS (lithium bis(trimethylsilyl)amide) (15.3 mL, 15.3 mmol) in THF was charged at a rate such that the temperature remained between -70 and -78.degree. C. After addition of the base was complete, the reaction mixture was warmed to .about.-45.degree. C. over .about.15 minutes. The stirred reaction was quenched at -70.degree. C by slow addition of sat. aq. NH.sub.4Cl (7.5 mL) solution and water (38 mL). The dry ice bath was removed and the solution was warmed to 20-25.degree. C. from the reaction mixture. Ethyl acetate (50 mL) was added, the mixture agitated, and layers separated. The organic layer was washed with saturated sodium bicarbonate solution (2.times.38 mL) followed by brine (25 mL) and concentrated to a volume of 50 mL. Acetonitrile (50 mL) was added and the solution was concentrated to a volume of 50 mL. This step was repeated. Water (.about.5-6 mL) was slowly added to the hot solution (60-70.degree. C.) until the cloud point was reached. The thin slurry was held for 30 min at high temperature and then slowly cooled over several hours with stirring. The product was filtered, cake was washed with a 5:1 mixture of acetonitrile and water, and dried to afford 7.5 g (91%) of the title compound as a white crystalline material.

Detail Description Paragraph - DETX (80):

[0424] was transferred to a 5.0-liter round bottom flask equipped with a mechanical stirrer, a thermometer, and a septa. While temperature was controlled at <29.degree. C., 1 N HCl (aq) was added to the above aqueous layer until the pH=6.94. Subsequently, 330 mL of ethyl acetate was added to the aqueous layer followed by charging more 1 N HCl (aq) until pH=2.82. After separating and saving the ethyl acetate layer, the aqueous layer was extracted with ethyl acetate (330 mL.times.3). The combined ethyl acetate layers containing acid lb.sup.8 of the invention 75

Detail Description Paragraph - DETX (81):

[0425] were washed with 50% brine (265 mL), brine (427 mL), separated and mixed with a suspension of L-arginine (27.4 g, 157 mmol) in ethanol (276 mL) and water (138 mL). The mixture was evaporated to dryness under reduced pressure at ca 45-50.degree. C. To the resulting white solid were added ethyl acetate (450 mL), ethanol (316 mL), and water (145 mL) followed by heating the white suspension to 50.degree. C. Another 36.7 mL of water was added to dissolve all solids at 56.degree. C; subsequently 1720 mL of ethy acetate was added to the hot solution to initialize the crystallization. The white suspension was stirred at 50.degree. C. for 1.5 h and at ambient for 13 h. After filtration, the crystalline solid was washed with 143 mL of a mixture of EtOAc (200 mL), EtOH (12 mL) and H.sub.2O (6 mL) and was dried in vacuo at 40-50.degree. C. for 24 h. The title product obtained as a white solid weighed

78.9 (g). Yield, 75.7%.  $[\alpha]_D^{25} = +23.0$  (c 0.31, CH<sub>2</sub>Cl<sub>2</sub>:H<sub>2</sub>O, 1:1, v/v).

Claims Text - CLTX (37):

36. The combination as defined in claim 17 wherein the other therapeutic agent is an anti-Alzheimer's agent or anti-dementia agent, which is tacrine HCl (Cognex.RTM.), donepezil (Aricept.RTM.), a  $\gamma$ -secretase inhibitor, a  $\beta$ -secretase inhibitor and/or antihypertensive agent; an antiosteoporosis agent, which is parathyroid hormone, a bisphosphonate, alendronate, a Ca receptor agonist or a progestin receptor agonist; a hormone replacement therapeutic agent, which is a selective estrogen receptor modulator (SERM); a tyrosine kinase inhibitor; a selective androgen receptor modulator; an antiarrhythmic agent, which is a  $\beta$ -blocker, or a calcium channel blocker, or an  $\alpha$ -adrenergic blocker; coenzyme Q sub. 10; an agent that upregulates type III endothelial cell nitric acid synthase; a chondroprotective compound which is polysulfated glycosaminoglycan (PSGAG), glucosamine, chondroitin sulfate (CS), hyaluronic acid (HA), pentosan polysulfate (PPS), doxycycline or minocycline; a cyclooxygenase (COX)-2 inhibitor, which is Celebrex.RTM. (Searle) or Vioxx.RTM. (Merck) or a glycoprotein IIa/IIIb receptor antagonist; a 5-HT reuptake inhibitor; a growth hormone secretagogue; an anti-atherosclerosis agent; an anti-infective agent, or an immunosuppressant for use in transplantation, or an antineoplastic agent.

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ABSTRACT:

Compounds of the following structure are HMG CoA reductase inhibitors and thus are active in inhibiting cholesterol biosynthesis, modulating blood serum lipids, for example, lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, dyslipidemia, hormone replacement therapy, hypercholesterolemia, hypertriglyceridemia and atherosclerosis as well as Alzheimer's disease and osteoporosis 1

and pharmaceutically acceptable salts thereof, 2

n is 0 or 1;

x is 0, 1, 2, 3 or 4;

y is 0, 1, 2, 3 or 4, provided that at least one of x and y is other than 0;

and optionally one or more carbons of (CH.sub.2), and/or (CH.sub.2).sub.y

together with additional carbons form a 3 to 7 membered spirocyclic ring;

R.sub.1 and R.sub.2 are the same or different and are independently selected

from alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or

cycloheteroalkyl;

R.sub.3 is H or lower alkyl;

R.sub.4 and R.sub.7 are as defined herein.

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Summary of Invention Paragraph - BSTX (168):



[0164] Referring to Scheme 5, the arginine salt of the compounds of formula I of the invention may be prepared by treating alkali metal salt (preferably sodium) Ib with acid (TFA, HCl) to form the acid Ib.sup.6 which is treated with arginine in the presence of suitable solvents such as ethyl alcohol and H.sub.2O, ethyl acetate, acetonitrile and the like, to form arginine salt Ib.sup.7. 25

Summary of Invention Paragraph - BSTX (189):

[0185] The squalene synthetase inhibitors suitable for use herein include, but are not limited to, .alpha.-phosphono-sulfonates disclosed in U.S. Pat. No. 5,712,396, those disclosed by Biller et al, J. Med. Chem., 1988, Vol. 31, No. 10, pp 1869-1871, including isoprenoid (phosphinyl-methyl)phosphonates as well as other known squalene synthetase inhibitors, for example, as disclosed in U.S. Pat. No. 4,871,721 and 4,924,024 and in Biller, S. A., Neuenschwander, K., Ponpipom, M. M., and Poulter, C. D., Current Pharmaceutical Design, 2, 1-40 (1996).

Summary of Invention Paragraph - BSTX (204):

[0200] an anti-oxidant such as beta-carotene, ascorbic acid, .alpha.-tocopherol or retinol as disclosed in WO 94/15592 as well as Vitamin C and an antihomocysteine agent such as folic acid, a folate, Vitamin B6, Vitamin B12 and Vitamin E;

Summary of Invention Paragraph - BSTX (284):

[0280] a chondroprotective compound such as a polysulfated glycosaminoglycan (PSGAG), glucosamine, chondroitin sulfate (CS), hyaluronic acid (HA), pentosan polysulfate (PPS), doxycycline or minocycline, such as disclosed in EP 970694;

Summary of Invention Paragraph - BSTX (361):

[0357] To a stirred solution of crude Part C compound (26.9 mmol) in HOAc (128 mL) was added ammonium acetate (9.14 g, 118.6 mmol) and copper (II) acetate monohydrate (19.7 g, 99.7 mmol). The reaction mixture was heated at reflux under argon overnight. After cooling to room temperature, the reaction mixture was poured into a mixture of NH.sub.4OH (150 mL) and ice (.about.300 g), then extracted with Et.sub.2O (3.times.100 mL). The combined Et.sub.2O extracts were washed with H.sub.2O and brine, then dried (Na.sub.2SO.sub.4), filtered and concentrated in vacuo. Purification by flash chromatography (2:20:80-EtOAc/CH.sub.2Cl.sub.2/hexane) gave the title compound as a white foam, 7.7 g, 71% yield (from Part B compound). 35

Detail Description Paragraph - DETX (4):

[0366] A 1 L 3-necked round bottom flask was flame-dried and then fitted with a mechanical stirrer, an argon-filled balloon, vacuum take-off and a thermocouple. To a stirred slurry of Part (1) compound (7.00 g, 12.9 mmol) in THF (200 mL) at 0.degree. C. was added n-butyllithium solution (5.4 mL, 2.5 M in hexanes, 13.5 mmol) over 20 min. A deep red-orange solution formed. After 30 min, a solution of zinc chloride-N,N,N',N'-tetramethylethylene-diamine complex (dried in vacuo at 60.degree. C. for 2h, 3.42 g, 13.5 mmol) in THF

(100 mL) was added via cannula and stirred 30 min. After 30 min, the resulting solution was cannulated into a solution of Example 2 Part G aldehyde (4.30 g, 16.6 mmol) in THF (20 mL) at room temperature over 20 min. A light orange solution soon formed, followed by a precipitate. After 3 h, the reaction was quenched with brine (50 mL) and water (50 mL) and extracted three times with ethyl acetate (100 mL). The organic extracts were combined, dried (MgSO<sub>4</sub>) and evaporated. LCMS of the crude material indicated unreacted Part (1) compound and an 89/11 mixture of the desired (E) isomer/undesired (Z) isomer.

Detail Description Paragraph - DETX (8):

[0369] To a solution of 4-fluoro-benzaldehyde (5 g, 40.3 mmol) and ethyl isobutyryl acetate (6.5 mL, 40.3 mmol) in benzene (50 mL) was added piperidine (400  $\mu$ L, 4.04 mmol), followed by acetic acid (100  $\mu$ L, 1.66 mmol). The reaction was refluxed for 16 hours and partitioned between aqueous HCl (1N, 20 mL) and ethyl acetate (50 mL  $\times$  2). The combined organic layers were washed with saturated NaHCO<sub>3</sub> (20 mL), brine (10 mL), and dried over sodium sulfate (Na<sub>2</sub>SO<sub>4</sub>). The solvent was removed in vacuo. Distillation at 140.degree. C. at 300 mm Hg afford 9.06 g (85% yield) of compound A as a yellow oil. ESI-LC/MS (M+H)<sup>+</sup>=264. 44

Detail Description Paragraph - DETX (10):

[0371] To a solution of the crude compound B (12 g) in aqueous HOAc (100 mL) was added ammonium acetate (9.5 g, 123.2 mmol), followed by cupric acetate monohydrate (20.7g, 113.9 mmol). The reaction was reflux for 20 hours, cooled to room temperature, then poured into a solution of ammonium hydroxide in ice (1 to 1; v/v). The aqueous layer was extracted with ethyl ether (200 mL  $\times$  3). The combined organic layers were washed with water (50 mL) and brine (50 mL). Flash chromatography (10% ethyl acetate in hexane) afforded 10.2 g (88% yield) of compound C as white powder. ESI-LC/MS (M+H)<sup>+</sup>=404; m.p. 138-140.degree. C. 46

Detail Description Paragraph - DETX (11):

[0372] To a solution of compound C (10 g, 24.78 mmol) in anhydrous THF (240 mL) at 0.degree. C. was added 1.0 M lithium aluminum hydride in THF (74 mL, 74 mmol). The reaction was stirred at 0.degree. C. for 1 hour and then warmed to room temperature and stirred for 16 hours. The reaction was then cooled to 0.degree. C. and quenched slowly with ice, then sodium hydroxide (10% NaOH, 20 mL). The mixture was extracted with diethyl ether (50 mL  $\times$  2) and filtered. The filter cake was then washed with more ethyl ether (10 mL) and ethyl acetate (10 mL). The combined organic layers were washed with water (10 mL) and brine (10 mL), then dried over sodium sulfate (Na<sub>2</sub>SO<sub>4</sub>). Flash chromatography (20% ethyl acetate in hexane) afforded 6.5 g (73% yield) of compound D. ESI-LC/MS (M+H)<sup>+</sup>=362; m.p. 170-171.degree. C. 47

Detail Description Paragraph - DETX (12):

[0373] To a solution of compound D (8.5 g, 23.54 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (100 mL) at 0.degree. C. was slowly added 1.0 M phosphorous tribromide in CH<sub>2</sub>Cl<sub>2</sub> (47 mL, 47.1 mmol) while maintaining the temperature below 10.degree. C. After the addition was complete, the reaction

was stirred at 0.degree. C. for 1 hour and then poured into saturated cold NaHCO.sub.3 solution (200 mL) with stirring. The aqueous layer was extracted with CH.sub.2Cl.sub.2 (50ml.times.2) and the combined organic layer was washed with water (10 mL) and brine (10 mL), then dried over sodium sulfate (Na.sub.2SO.sub.4). Flash chromatography (10% ethyl acetate in hexane) gave 8.6 g (86% yield) of compound E as a white solid. ESI-LC/MS (M+H).sup.+ = 424; m.p. 157-159.degree. C. 48

Detail Description Paragraph - DETX (13):

[0374] To a solution of diethyl phosphite (785 .mu.L, 6.09 mmol) in anhydrous THF (25 mL) at -10.degree. C. under argon was added a 1.0 M THF solution of sodium hexamethyldisazide (6 mL, 6.09 mmol). The reaction mixture was stirred at -10.degree. C. for 30 minutes. A solution of compound E (2.15 g, 5.08 mmol) in THF was added to the reaction while maintaining the temperature at -10.degree. C. After the addition was complete, the reaction was stirred for 1 hour and quenched with water (20 mL). The aqueous layer was extracted with ethyl acetate (30 mL.times.2) and the combined organic layers were washed with 1N HCl solution (5 mL). The organic solvent was removed in vacuo. Flash chromatography using 20% to 30% ethyl acetate in hexane as eluting afforded 2.29 g (94% yield) of compound F as a white solid. ESI-LC/MS (M+H).sup.+ = 482; m.p. 102-105.degree. C. 49

Detail Description Paragraph - DETX (16):

[0377] To a cooled (-78.degree. C.) solution of compound F (2.02 g, 4.19 mmol) in anhydrous THF (30 mL) under argon was slowly added a 2.5 M THF solution of n-butyllithium (2.1 mL) over a period of 40 minutes. The temperature was maintained below -75.degree. C. during the addition. After the addition was complete, the reaction mixture was stirred for another 40 minutes at -78.degree. C. A solution of compound G (2.2 g, 8.52 mmol) in THF under argon was cannulated into the phosphonate mixture at -78.degree. C. After the addition was complete, the reaction was stirred for 1 hour at -78.degree. C. The reaction was then warmed to -10.degree. C. and stirred for 1 hour and then stirred at room temperature for an additional hour. The mixture was quenched with saturated ammonium chloride solution (5 mL) and extracted with ethyl acetate (60 mL.times.3). The combined organic layers were washed with water (10 mL) and brine (10 mL), then dried over sodium sulfate (Na.sub.2SO.sub.4) and filtered. The filtrate was concentrated in vacuo. Flash chromatography using 5% to 10% ethyl acetate in hexane as eluent afforded 1.48 g (60% yield) of compound H as a white solid. ESI-LC/MS (M+H).sup.+ = 586; m.p. 148-149.degree. C. 51

Detail Description Paragraph - DETX (17):

[0378] To a cooled (0.degree. C.) solution of compound H (500 mg, 0.854 mmol) in anhydrous CH.sub.2Cl.sub.2 (12 mL) under argon was slowly added trifluoroacetic acid (987 mL, 12.82 mmol). After the addition was complete, the reaction mixture was allowed to stirred at 0.degree. C. for 10 minutes and at room temperature for 3 hours and then the solvent was removed in vacuo. The reaction mixture was quenched with phosphate solution (pH 7.5, 12 mL) and extracted with CH.sub.2Cl.sub.2 (20 mL.times.2). The combined organic layers were washed with brine (10 mL), dried over sodium sulfate (Na.sub.2SO.sub.4),

and filtered. The solvent was removed in vacuo. Flash silica gel chromatography using 30% to 50% ethyl acetate in hexane as an eluent afforded 331mg (80% yield) of compound I as a white powder. ESI-LC/MS (M+H).sup.+=588; m.p.=199-200.degree. C. 52

Detail Description Paragraph - DETX (25):

[0385] To part H(I) compound (109 mg, 0.2 mmol) in 25 mL 2-necked round bottom flask (flame-dried and fitted with an argon-filled balloon, vacuum take-off and a thermocouple) was added 0.5 mL of DMPU (distilled over CaH.sub.2 under reduced pressure, stored with 4A molecular sieves). The resulting slurry was warmed while stirring until becoming a clear solution, which was diluted with THF (1.5 mL). The reaction mixture was evacuated and purged three times with argon, then cooled to -78.degree. C. To the cooled reaction mixture was added dropwise 0.42 mL of a 0.5 M solution of LDA in THF.sup.1 (0.21 mmol). An amber colored solution formed. After stirring at -78.degree. C. for 30 minutes, a solution of Example 2 Part G aldehyde (67 mg, 0.26 mmol) in THF (0.5 mL) was added via a syringe. After addition, the resulting yellow solution was stirred at -78.degree. C. for 30 minutes, then at 0.degree. C. for 1 hour before quenched with an aqueous solution of ammonium chloride. The reaction mixture was extracted three times with ethyl acetate (10 mL). The organic extracts were combined, washed with water and brine, dried (MgSO.sub.4) and evaporated. The crude product was purified using flash chromatography on silica gel eluting with 5% EtOAc/hexane. The desired fractions were pooled and concentrated, and the collected residue dried in vacuo overnight to give Part H(2) compound as a white foam, 80 mg (68% yield).

Detail Description Paragraph - DETX (30):

[0389] To a cooled (0.degree. C.) solution of Part A compound (450mg, 0.766 mmol) in anhydrous CH.sub.2Cl.sub.2 (9 mL) under argon was slowly added trifluoroacetic acid (886 mL, 12.5 mmol). After the addition was complete, the reaction mixture was allowed to stirred at 0.degree. C. for 10 minutes and at room temperature for 3 hours and then the solvent was removed in vacuo. The reaction mixture was quenched with phosphate solution (pH 7.51 12 mL) and extracted with CH.sub.2Cl.sub.2 (20 mL.times.2). The combined organic layer was washed with brine (saturated NaCl solution, 10 ml), dried over sodium sulfate (Na.sub.2SO.sub.4) and filtered. The solvent was removed in vacuo. Flash silica gel chromatography using 30% to 50% ethyl acetate in hexane as an eluent afford 330mg (91% yield) part B compound as a white powder. ESI-LC/MS (M+H).sup.+=474, MP (.degree. C.)=253-254. 57

Detail Description Paragraph - DETX (44):

[0400] To a mixture of 4-fluoro-benzaldehyde (935.8 g, 7.54 moles) and methyl isobutyryl acetate (1087 g, 7.54 moles) was added piperidine (64.2 g, 0.75 mol), followed by acetic acid (22.6 g, 0.38 mol). The mixture was heated to 80 to 85.degree. C. for about 2 hours. 16 Liters (4.times.4 L) of toluene was added and mixed with the reaction mixture. The toluene was removed using a rotavapor (50-65.degree. C./20-90 torr), leaving a yellow oil. The yellow oil was dissolved in 5 L MTBE and washed with:

Detail Description Paragraph - DETX (50):

[0406] To a solution of the crude compound B (3078 g) in aqueous HOAc (16 L) was added ammonium acetate (1446 g), followed by cupric acetate monohydrate (1859 g). The reaction was refluxed between 120 to 124.degree. C. for 12-15 hours. Approximately 90% of the acetic acid was evaporated to produce a green slurry. The slurry was then mixed with 14 L MTBE.

Detail Description Paragraph - DETX (56):

[0412] To a 500 mL round bottom flask equipped with a magnetic stirrer and a nitrogen inlet was charged Part C compound (17) (Scheme 6) (50.0 g, 128.4 mmol) and toluene (170 mL). The mixture was stirred at 20-25.degree. C. until a clear solution was obtained. A solution of 65% Red-Al in toluene (57.8 mL, 192.6 mmol) was added and the reaction mixture was heated to 80.degree. C. until complete as determined by HPLC. The reaction mixture was cooled to -20.degree. C. and quenched by pouring it into cold (0-5.degree. C.) 20% HCl (495 mL). Phases were separated and the spent toluene phase was discarded. The pH of the aqueous phase was adjusted from <0 to 4-5 with 10N NaOH. Ethyl acetate (500 mL) was added and the pH adjustment continued to 7-8. The phases were separated. The aqueous phase was extracted with additional ethyl acetate (2.times.500 mL). The combined rich ethyl acetate solution was washed with water (3.times.250 mL) and concentrated under reduced pressure to ~465 mL. This solution was carried through to the next oxidation step.

Detail Description Paragraph - DETX (57):

[0413] The rich ethyl acetate solution was charged from above into a three neck 1-L flask equipped with mechanical stirring, temperature controller, and addition funnel and cooled to 0-5.degree. C. To the slurry, potassium bromide (1.53 g, 12.8 mmol) and TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) (0.20 g, 1.28 mmol) were added. The pH of NaOCl (sodium hypochlorite) solution (212.1 mL) was adjusted to -9.1 and added to the slurry at a rate such that the temperature remained at 0-5.degree. C. Stirring was continued at 0-5.degree. C. until the reaction was complete as determined by HPLC. The aqueous phase was extracted with EtOAc (2.times.200 mL). The combined rich organic phase was washed with a 1:1 solution of sat. aq. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (sodium thiosulfate) (75 mL) and water (75 mL) followed by wash of the rich organic phase with 1N NaOH (250 mL). The rich organic phase was washed with water (250 mL) and concentrated to ~100 mL under reduced pressure. Isopropanol (IPA) (400 mL) was added and the resulting mixture was heated to reflux (80-85.degree. C.). The solution was distilled to a volume of ~250 mL. Water (50 mL) was added and the crystal slurry was stirred at 70-80.degree. C. for 1 h then allowed to cool to 20-25.degree. C. over at least 1 h. The slurry was held at 20-25.degree. C. for at least 1 h before collecting the solid by filtration on a Buchner funnel. The cake was washed with cold (0.degree. C.) IPA/water (4:1) (2.times.50 mL) and dried to a constant weight under vacuum at 40.degree. C. to afford 41.5 g (90%) of title aldehyde as a white crystalline solid.

Detail Description Paragraph - DETX (64):

[0418] An N<sub>2</sub> purged 250 mL 3-neck rb flask was charged with Example 35 pyridine derivative (18) (5.0 g, 13.9 mmol), Example 36 sulfone (16) (6.92 g, 15.3 mmol) and THF (75 mL). The stirred solution was cooled to -74 to

-78.degree. C. Slowly a 1M solution of LIHMDS (lithium bis(trimethylsilyl)amide) (15.3 mL, 15.3 mmol) in THF was charged at a rate such that the temperature remained between -70 and -78.degree. C. After addition of the base was complete, the reaction mixture was warmed to -45.degree. C. over -15 minutes. The stirred reaction was quenched at -70.degree. C. by slow addition of sat. aq. NH<sub>4</sub>Cl (7.5 mL) solution and water (38 mL). The dry ice bath was removed and the solution was warmed to 20-25.degree. C. from the reaction mixture. Ethyl acetate (50 mL) was added, the mixture agitated, and layers separated. The organic layer was washed with saturated sodium bicarbonate solution (2.times.38 mL) followed by brine (25 mL) and concentrated to a volume of 50 mL. Acetonitrile (50 mL) was added and the solution was concentrated to a volume of 50 mL. This step was repeated. Water (.about.5-6 mL) was slowly added to the hot solution (60-70.degree. C.) until the cloud point was reached. The thin slurry was held for 30 min at high temperature and then slowly cooled over several hours with stirring. The product was filtered, cake was washed with a 5:1 mixture of acetonitrile and water, and dried to afford 7.5 g (91%) of the title compound as a white crystalline material.

Detail Description Paragraph - DETX (69):

[0422] was transferred to a 5.0-liter round bottom flask equipped with a mechanical stirrer, a thermometer, and a septa. While temperature was controlled at <29.degree. C., 1 N HCl (aq) was added to the above aqueous layer until the pH=6.94. Subsequently, 330 mL of ethyl acetate was added to the aqueous layer followed by charging more 1 N HCl (aq) until pH=2.82. After separating and saving the ethyl acetate layer, the aqueous layer was extracted with

Detail Description Paragraph - DETX (70):

[0423] ethyl acetate (330 mL.times.3). The combined ethyl acetate layers containing acid lb.sup.8 of the invention 70

Detail Description Paragraph - DETX (71):

[0424] were washed with 50% brine (265 mL), brine (427 mL), separated and mixed with a suspension of L-arginine (27.4 g, 157 mmol) in ethanol (276 mL) and water (138 mL). The mixture was evaporated to dryness under reduced pressure at ca 45-50.degree. C. To the resulting white solid were added ethyl acetate (450 mL), ethanol (316 mL), and water (145 mL) followed by heating the white suspension to 50.degree. C. Another 36.7 mL of water was added to dissolve all solids at 56.degree. C.; subsequently 1720 mL of ethyl acetate was added to the hot solution to initialize the crystallization. The white suspension was stirred at 50.degree. C. for 1.5 h and at ambient for 13 h. After filtration, the crystalline solid was washed with 143 mL of a mixture of EtOAc (200 mL), EtOH (12 mL) and H<sub>2</sub>O (6 mL) and was dried in vacuo at 40-50.degree. C. for 24 h. The title product obtained as a white solid weighed 78.9 (g). Yield, 75.7%. [ $\alpha$ ]<sub>D</sub><sup>25</sup>=+23.0 (c 0.31, CH<sub>2</sub>Cl<sub>2</sub>:H<sub>2</sub>O, 1:1, v/v).

Claims Text - CLTX (37):

36. The combination as defined in claim 17 wherein the other therapeutic agent is an anti-Alzheimer's agent or anti-dementia agent, which is tacrine HCl (Cognex.RTM.), donepezil (Aricept.RTM.), a .gamma.-secretase inhibitor, a .beta.-secretase inhibitor and/or antihypertensive agent; an antiosteoporosis agent, which is parathyroid hormone, a bisphosphonate, alendronate, a Ca receptor agonist or a progestin receptor agonist; a hormone replacement therapeutic agent, which is a selective estrogen receptor modulator (SERM); a tyrosine kinase inhibitor; a selective androgen receptor modulator; an antiarrhythmic agent, which is a .beta.-blocker, or a calcium channel blocker, or an .alpha.-adrenergic blocker; coenzyme Q sub. 10; an agent that upregulates type III endothelial cell nitric acid syntase; a chondroprotective compound which is polysulfated glycosaminoglycan (PSGAG), glucosamine, chondroitin sulfate (CS), hyaluronic acid (HA), pentosan polysulfate (**PPS**), doxycycline or minocycline; a cyclooxygenase (COX)-2 inhibitor, which is Celebrex.RTM. (Searle) or Vioxx.RTM. (Merck) or a glycoprotein IIa/IIIb receptor antagonist; a 5-HT reuptake inhibitor; a growth hormone secretagogue; an anti-atherosclerosis agent; an anti-infective agent, or an immunosuppressant for use in transplantation, or an antineoplastic agent.

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ABSTRACT:

Compounds of the following structure are HMG CoA reductase inhibitors and thus are active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and atherosclerosis 1 and pharmaceutically acceptable salts thereof, wherein X is O or S; 2 n is 0 or 1; R.sub.1 and R.sub.2 are the same or different and are independently selected from alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroalkyl; and R.sub.3 to R.sub.9 are as defined herein.

[0001] This application claims priority from U.S. provisional application No. 60/211,595, filed Jun. 15, 2000.

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Detail Description Paragraph - DETX (78):

[0178] The squalene synthetase inhibitors suitable for use herein include, but are not limited to,  $\alpha$ -phosphono-sulfonates disclosed in U.S. Pat. No. 5,712,396, those disclosed by Biller et al, J. Med. Chem., 1988, Vol. 31, No.



10, pp 1869-1871, including isoprenoid (phosphinyl-methyl)phosphonate- s as well as other known squalene synthetase inhibitors, for example, as disclosed in U.S. Pat. No. 4,871,721 and 4,924,024 and in Biller, S.A., Neuenschwander, K., Ponpipom, M.M., and Poulter, C.D., Current Pharmaceutical Design, 2, 1-40 (1996).

Detail Description Paragraph - DETX (93):

[0193] an anti-oxidant such as beta-carotene, ascorbic acid, .alpha.-tocopherol or retinol as disclosed in WO 94/15592 as well as Vitamin C and an antihomocysteine agent such as folic acid, a folate, Vitamin B6, Vitamin B12 and Vitamin E;

Detail Description Paragraph - DETX (173):

[0273] a chondroprotective compound such as a polysulfated glycosaminoglycan (PSGAG), glucosamine, chondroitin sulfate (CS), hyaluronic acid (HA), pentosan polysulfate (PPS), doxycycline or minocycline, such as disclosed in EP 970694;

Detail Description Paragraph - DETX (254):

[0353] A mixture of crude Part B compound (17.0 g, 27.3 mmol), ammonium acetate (9.34 g, 120 mmol) and copper acetate monohydrate (20.54 g, 101 mmol) in glacial acetic acid (100 ml) was refluxed under argon for 19 hours. The mixture was poured into an ice-cold solution of concentrated ammonium hydroxide (85 ml) in water (170 ml) and the bright blue solution was extracted with ether (3.times.200 ml). The combined organic extracts were washed with water (2.times.80 ml) and brine (80 ml), dried (anhydrous Na.sub.2SO.sub.4), filtered, evaporated to dryness, and dried in vacuo. The crude product (14 g, brown syrup) was chromatographed in two batches, each on a silica gel column (EM, 2-1/4".times.10") to give the desired product as an off-white solid (4.161 g). An additional 931 mg of product was obtained from chromatography of mixed fractions. Yield: 5.092 g, 46% from compound A). Rf 0.53 (Silica gel; EtOAc:Hexane-1:4; UV) 36

Detail Description Paragraph - DETX (255):

[0354] A solution of Part C compound (2.515 g, 6.23 mmol) in dry THF (30 ml) was cooled to 0.degree. C. (ice-water bath), treated dropwise with lithium aluminum hydride (1.0 M in THF; 12.5 ml, 12.5 mmol), stirred at 0.degree. C. for 30 minutes then at room temperature for 3 hours. The reaction mixture was cooled to 0.degree. C. treated successively with water (0.5 ml), 15% NaOH (0.5 ml) and water (1.5 ml), stirred at room temperature for 5 minutes then diluted with ethyl acetate (50 ml). The slurry was filtered through a Celite.RTM. pad, washing the pad well with ethyl acetate (3.times.25 ml). The clear filtrate was evaporated to dryness and dried in vacuo to give the title product. Yield: 2.386 g, white foam (100%). Rf 0.15 (Silica gel; EtOAc:Hexane-1:4; UV). 37

Detail Description Paragraph - DETX (256):

[0355] A solution of Part D compound (2.27 g, 6.23 mmol) in dry dichloromethane (45 ml) was cooled to 0.degree. C. (ice-water bath) and

treated dropwise with phosphorus tribromide (1.0 M in dichloromethane; 12.5 ml, 12.5 mmol). The ice bath was removed and the reaction mixture was stirred at room temperature for 30 minutes after which it was re-cooled to 0.degree. C. and treated dropwise with saturated sodium bicarbonate (70 ml). The mixture was then warmed to room temperature and extracted with ethyl acetate (2.times.100 ml). The combined organic extracts were washed with water (2.times.50 ml) and brine (50 ml), re-extracting each aqueous wash with dichloromethane (100 ml). The organic extracts were dried (anhydrous sodium sulfate), filtered, evaporated to dryness and dried in vacuo to give the title product as a white solid. Yield: 2.503 g, (94%). m.p.=169-171.degree. C. Rf 0.58 (Silica gel; EtOAc:Hexane-1:4; UV). 38

Detail Description Paragraph - DETX (257):

[0356] A solution of diethyl phosphite (0.88 ml, 6.83 mmoles) in dry THF (10 ml) was cooled to -10.degree. C. (acetonitrile-dry ice bath), treated with sodium (bistrimethylsilyl)amide (1.0 M in THF; 6.7 ml, 6.7 mmol) and stirred at -10.degree. C. for 30 minutes. The cooled solution was treated with a solution of Part E compound (2.41 g, 5.68 mmol) in dry THF (20 ml), stirred at -10.degree. C. for 1.0 hour then quenched at -10.degree. C. with water (14 ml). The solution was extracted with ethyl acetate (2.times.75 ml) and the combined organic extracts washed with 1.0 M hydrochloric acid (8.0 ml) and brine (10 ml), dried (anhydrous sodium sulfate), filtered, evaporated to dryness and dried in vacuo. The crude product (3.12 g, syrup) was chromatographed on a silica gel column (EM, 5.5 cm.times.12.5 cm) to give the title compound as a syrup. Yield: 2.34 g (85.5%). Rf 0.33 (Silica gel; EtOAc:Hexane-1:1; UV). 39

Detail Description Paragraph - DETX (258):

[0357] A solution of Part F compound (2.29 g, 4.756 mmol) in dry THF (20 ml) was cooled to -78.degree. C., treated with 2.37 M n-butyllithium (2.41 ml, 5.71 mmol) and stirred at -78.degree. C. for 40 minutes. The solution was treated dropwise via cannula with a -78.degree. C. solution of Part A(1) compound (2.36 g, 9.15 mmol) in dry THF (10 ml), keeping both solutions at -78.degree. C. at all times. The reaction mixture was stirred at -78.degree. C. for 1.0 hr, -10.degree. C. for 1.0 hr and at room temperature for 5 hr, quenched with 25% ammonium chloride solution (12 ml) then extracted with ethyl acetate (2.times.100 ml). The combined organic extracts were washed with 25% ammonium chloride solution (12 ml) and brine (12 ml), dried (anhydrous sodium sulfate), filtered, evaporated to dryness and dried in vacuo. The crude product yellow syrup was chromatographed on a silica gel column (EM, 2-1/4".times.10") to afford the title compound as a syrup. Yield: 878 mg (32%). Rf 0.37 (Silica gel; EtOAc:Hexane-1:4; UV). 40

Detail Description Paragraph - DETX (259):

[0358] A solution of Part G compound (850 mg, 1.45 mmol) in dry dichloromethane (20 ml) was cooled to 0.degree. C., treated with trifluoroacetic acid (1.85 ml, 24 mmol), stirred at 0.degree. C. for 5 minutes, then at room temperature for 4.5 hours. The reaction mixture was poured slowly into a 1 L flask containing ethyl acetate (300 ml) and saturated sodium bicarbonate (40 ml), rinsing the flask with ethyl acetate (50 ml). The

mixture was stirred well and the phases separated, washing the organic phase with saturated sodium bicarbonate (25 ml) and brine (25 ml). The organic phase was dried over anhydrous sodium sulfate, filtered, evaporated to dryness and dried in vacuo. The crude product mixture was chromatographed on a silica gel column (EM, 1.5".times.12") to give the desired compound as a syrup. Yield: 570 mg (83%). Rf 0.23 (Silica gel; EtOAc:Hexane-1:1; UV) 41

Detail Description Paragraph - DETX (305):

[0401] (50 g, 128.4 mmol) (prepared as described in Example 2 Parts A, B and C except methyl isobutyryl acetate is substituted for ethyl isobutyryl acetate) and toluene (170 mL). The mixture is stirred at 20-25.degree. C. until a clear solution is obtained. A solution of 65% Red-Al in toluene (57.8 mL, 192.6 mmol) is added and the reaction mixture is heated to 80.degree. C. until complete as determined by HPLC. The reaction mixture is cooled to .about.20.degree. C. and quenched by pouring it into cold (0-5.degree. C. ) 20% HCl (495 mL). Phases are separated and the spent toluene phase is discarded. The pH of the aqueous phase is adjusted from <0 to 4-5 with 10N NaOH. Ethyl acetate (500 mL) is added and the pH adjustment continued to 7-8. The phases are separated. The aqueous phase is extracted with additional ethyl acetate (2.times.500 mL). The combined rich ethyl acetate solution is washed with water (3.times.250 mL) and concentrated under reduced pressure to .about.465 mL. This solution is carried through to the next oxidation step.

Detail Description Paragraph - DETX (306):

[0402] The rich ethyl acetate solution is charged from above into a three neck 1-L flask equipped with mechanical stirring, temperature controller, and addition funnel and cooled to 0-5.degree. C. To the slurry, potassium bromide (1.53 g, 12.8 mmol) and TEMPO (2,2,6,6-tetramethyl-1-piperidinylo- xy) (0.20 g, 1.28 mmol) are added. The pH of NaOCl (sodium hypochlorite) solution (212.1 mL) is adjusted to .about.9.1 and added to the slurry at a rate such that the temperature remained at 0-5.degree. C. Stirring is continued at 0-5.degree. C. until the reaction is complete as determined by HPLC. The aqueous phase is extracted with EtOAc (2.times.200 mL). The combined rich organic phase is washed with a 1:1 solution of sat. aq. Na.sub.2S.sub.2O.sub.3 (sodium thiosulfate) (75 mL) and water (75 mL) followed by wash of the rich organic phase with 1N NaOH (250 mL). The rich organic phase is washed with water (250 mL) and concentrated to .about.100 mL under reduced pressure. Isopropanol (IPA) (400 mL) is added and the resulting mixture is heated to reflux (80-85.degree. C.). The solution is distilled to a volume of .about.250 mL. Water (50 mL) is added and the crystal slurry is stirred at 70-80.degree. C. for 1 h then allowed to cool to 20-25.degree. C. over at least 1 h. The slurry is held at 20-25.degree. C. for at least 1 h before collecting the solid by filtration on a Buchner funnel. The cake is washed with cold (0.degree. C.) IPA/water (4:1) (2.times.50 mL) and dried to a constant weight under vacuum at 40.degree. C. to afford title aldehyde.

Detail Description Paragraph - DETX (316):

[0410] A.sub.n N.sub.2 purged 250 mL 3-neck rb flask is charged with Example 27 pyridine derivative (18) (5 g, 13.9 mmol), Example 28 sulfone (16) (6.9 g, 15.3 mmol) and THF (75 mL). The stirred solution is cooled to -74 to

-78.degree. C. Slowly a 1M solution of LiHMDS (lithium bis(trimethylsilyl)amide) (15.3 mL, 15.3 mmol) in THF is charged at a rate such that the temperature remained between -70 and -78.degree. C. After addition of the base is complete, the reaction mixture is warmed to about -45.degree. C. over about 15 minutes. The stirred reaction is quenched at -70.degree. C. by slow addition of sat. aq. NH<sub>4</sub>Cl (7.5 mL) solution and water (38 mL). The dry ice bath is removed and the solution is warmed to 20-25.degree. C. from the reaction mixture. Ethyl acetate (50 mL) is added, the mixture agitated, and layers separated. The organic layer is washed with saturated sodium bicarbonate solution (2.times.38 mL) followed by brine (25 mL) and concentrated to a volume of 50 mL. Acetonitrile (50 mL) is added and the solution is concentrated to a volume of 50 mL. This step is repeated. Water (about 5-6 mL) is slowly added to the hot solution (60-70.degree. C. ) until the cloud point is reached. The thin slurry is held for 30 min at high temperature and then slowly cooled over several hours with stirring. The product is filtered, cake is washed with a 5:1 mixture of acetonitrile and water, and dried to afford the title compound.

Claims Text - CLTX (37):

36. The combination as defined in claim 17 wherein the other therapeutic agent is an anti-Alzheimer's agent or anti-dementia agent, which is tacrine HCl (Cognex.RTM.), donepezil (Aricept.RTM.), a gamma-secretase inhibitor, a beta-secretase inhibitor and/or antihypertensive agent; an antiosteoporosis agent, which is parathyroid hormone, a bisphosphonate, alendronate, a Ca receptor agonist or a progestin receptor agonist; a hormone replacement therapeutic agent, which is a selective estrogen receptor modulator (SERM); a tyrosine kinase inhibitor; a selective androgen receptor modulator; an antiarrhythmic agent, which is a beta-blocker, or a calcium channel blocker, or an alpha-adrenergic blocker; coenzyme Q sub. 10; an agent that upregulates type III endothelial cell nitric acid synthase; a chondroprotective compound which is polysulfated glycosaminoglycan (PSGAG), glucosamine, chondroitin sulfate (CS), hyaluronic acid (HA), pentosan polysulfate (PPS), doxycycline or minocycline; a cyclooxygenase (COX)-2 inhibitor, which is Celebrex.RTM. (Searle) or Vioxx.RTM. (Merck) or a glycoprotein IIa/IIIb receptor antagonist; a 5-HT reuptake inhibitor; a growth hormone secretagogue; an anti-atherosclerosis agent; an anti-infective agent, or an immunosuppressant for use in transplantation, or an antineoplastic agent.

US-PAT-NO: 6572882

DOCUMENT-IDENTIFIER: US 6572882 B1

TITLE: Compositions based on resveratrol

DATE-ISSUED: June 3, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Vercauteren; Joseph	Pessac	N/A	N/A	FR
Castagnino; Chantal	Merignac	N/A	N/A	FR
Delaunay; Jean-Claude	Merignac	N/A	N/A	FR

APPL-NO: 09/ 462778

DATE FILED: January 19, 2000

PARENT-CASE:

The present application is a 371 PCT/FR 98/01548, filed Jul. 15, 1998.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
FR	97 08964	July 15, 1997

PCT-DATA:

APPL-NO: PCT/FR98/01548

DATE-FILED: July 15, 1998

PUB-NO: WO99/03816

PUB-DATE: Jan 28, 1999

371-DATE:

102(E)-DATE:

US-CL-CURRENT: 424/451, 424/489 , 514/733 , 514/734

ABSTRACT:

The invention relates to compositions based on derivatives of resveratrol having in particular a high stability as regards air and light.

15 Claims, 5 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 5

----- KWIC -----

Brief Summary Text - BSTX (41):

The process for obtaining monomers and oligomers of resveratrol, which is also envisaged by the invention, comprises the following stages extraction by addition, to the vine stalks, of water and/or of organic solvent(s), by subjecting the whole to a treatment such as maceration/lixiviation, ultrasonics or microwaves, delipidation before or after the extraction stage using a solvent of petroleum ether, hexane or chloroform type, additional extraction of the extract recovered by an organic solvent of ethyl acetate or ethyl ether type, concentration of the crude extract obtained, and, if desired, its lyophilization.

Brief Summary Text - BSTX (46):

High-performance results have been obtained with a hexane/ethyl acetate/ethanol/water mixture with for example the respective proportions of 6/48/11/42 or 4/5/3/3.

Brief Summary Text - BSTX (49):

Similarly, carbonylated or carboxylated solvents can be used instead of ethyl acetate, such as acetone, methylethylketone, methylisobutylketone, methylterbutylketone.

Brief Summary Text - BSTX (59):

These medicaments can also contain other active ingredients, in particular products with a protective effect vis-a-vis oxidation reactions. For example .beta.-carotene or vitamin E can be mentioned.

Detailed Description Text - DETX (6):

For example, the following are used: water; water/acetone 3/2 or 1/1; methanol; ethanol; water/ethanol: 1/1; water/ethyl acetate: 1/1; ethanol/acetone: 1/1; water/ethanol/acetone: 2/1/1, 1/2/1 or 1/1/2

Detailed Description Text - DETX (10):

This extract is in turn subjected to at least one other extraction stage. Ethyl acetate or ethyl ether is used at a rate of 3 to 5 times 100 ml.

Detailed Description Text - DETX (13):

FIG. 1 shows the HPLC chromatograph of an ethyl acetate extract obtained, after ultrasonic treatment for 2 hours, from 100 g of ground stalks (Merlot type) in 800 ml of water/acetone: 3/2, and delipidation with petroleum ether. Elution was carried out with A: H.sub.2 O/TFA; 100/0.0025 (TFA=trifluoroacetic acid) and B: MeOH/TFA 100/0.0025, according to the gradient

Detailed Description Text - DETX (19):

The extract obtained is then subjected to an extraction stage using ethyl acetate or ethyl ether as indicated previously for the preparation of extracts

using ultrasonics or microwaves.

Detailed Description Text - DETX (26):

Main Characteristics of the Device Rotational speed: 0-2000 rpm Column capacity: 230 ml Maximum pressure: 60.times.10.sup.5 Pa. Rotor material: polyphenylenesulphide (**PPS**) Partition disk: series of disks Partition cell: 2136 Cell length: 15 mm.

Detailed Description Text - DETX (27):

The stationary and mobile phases are respectively the lower and upper phases recovered after agitation and decantation of the hexane/ethyl acetate/ethanol/water mixture: 6/48/11/42, given the implementation of the technique in ascending mode in this example.

Detailed Description Text - DETX (32):

The 120 mg of ORs recovered in Example 2, dissolved in 2 ml of stationary phase, are separated in ascending mode. The stationary phase constitutes the lower phase of the hexane/ethyl acetate/ethanol/water mixture 4/5/3/3 and the mobile phase constitutes the upper phase of the same mixture. The rotational speed is 1100 rpm, the flow rate is 2 ml/minute and the pressure is 44.times.10.sup.5 Pa. Under these conditions, the fraction enriched in resveratrol is collected after 150 minutes of elution and the fraction enriched in resveratrol oligomers is collected after 240 minutes.

Detailed Description Text - DETX (106):

Perlaurate of ORs prepared according to Example 11 is mixed with selenium and vitamin E; Perlaurate of ORs: 85 mg (corresponding to 25 mg of ORs), DL-alpha.-tocopherol acetate: 40 mg, Selenium: 50 mg

US-PAT-NO: 6500463

DOCUMENT-IDENTIFIER: US 6500463 B1

TITLE: Encapsulation of sensitive components into a matrix to  
obtain discrete shelf-stable particles

DATE-ISSUED: December 31, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
van Lengerich; Bernhard H.	Plymouth	MN	N/A	N/A

APPL-NO: 09/ 410017

DATE FILED: October 1, 1999

US-CL-CURRENT: 424/499, 424/409, 424/410, 424/439, 424/488, 424/500  
, 424/501

ABSTRACT:

A solid active, sensitive encapsulant and/or a liquid encapsulant component which contains an active, sensitive encapsulant, is admixed with at least one plasticizable matrix material, a matrix component which is substantially non-plasticizable at temperatures lower than the decomposition temperature of the encapsulant and which increases the rate of release of the encapsulant from the matrix, and a liquid plasticizer to obtain a formable, extrudable, cuttable, mixture or dough. The matrix material is plasticized by the liquid plasticizer and the encapsulation of the active encapsulant, such as a live microorganism or an enzyme, is accomplished at a low temperature and under low shear conditions. The active component is encapsulated and/or embedded in the plasticizable matrix component or material in a continuous process to produce discrete, solid particles. The formable mixture may be obtained without or substantially no cooking or gelatinizing of the matrix ingredients. A solid encapsulant may be dry-blended with the plasticizable matrix material and the substantially non-plasticizable matrix material, followed by plasticization of the plasticizable matrix material.

92 Claims, 0 Drawing figures

Exemplary Claim Number: 1

----- KWIC -----

Brief Summary Text - BSTX (58):

Additional ingredients which may be used to control the release properties of the final product may be a hydrophobic agent for slowing down the rate of



release of the encapsulant. Exemplary of components which may be added to affect the hydrophobicity of the matrix include fats, oils, waxes, fatty acids, emulsifiers, such as mono- or di- glycerides, synthetic polymers such as polyolefins such as polyethylene or polypropylene, polyvinyl chloride, polyvinyl acetate and derivatives thereof, paraffin, and modified starches from plant sources that possess hydrophobic properties that are obtained via either physical or chemical modification, and mixtures of hydrophobic components. Plant lipids or synthetic lipids with melting points up to about 65.degree. C. may, for example, be employed as a hydrophobic agent. The hydrophobic components increase the hydrophobicity of the matrix and help to prevent or delay penetration of water or gastric juice into the matrix by repelling water or aqueous acids, thereby delaying the release of the encapsulant into the surrounding media.

Brief Summary Text - BSTX (67):

Exemplary of the active components which may be encapsulated or embedded in accordance with the present invention are: acepromazine, acetaminophen, acetohexamide, acetohydroxamic acid, acetylcholine, acetylcysteine acyclovir, albendazole, alclometasone dipropionate, allopurinol, alprazolam, alprostadil, amcinolide, amantadine, amdinocillin, amikacin amiloride, aminocaproic acid, aminophylline, aminosalicylate, aminosalicylic acid, amitriptyline hydrochloride, ammonium chloride, amobarbital, amodiaquine hydrochloride, amoxapine, amoxicillin, amphetamine sulfate, amphotericin, ampicillin amprolium, acetazolamide acetyldigoxin, acetylsalicylic acid, anileridine, anthralin, antipyrine, antivenin, apomorphine, apraclonidine, ascorbic acid, aspirin, acromycin atropine, amoxycillin anipamil, azaperone azatadine maleate, azathioprine, azithromycin, aztreonam, bacampicillin, bacitracin, baclofen, barium salts, beclomethasone dipropionate, belladonna extract, bendroflumethiazide, benoxinate hydrochloride, benzethonium chloride, benzocaine, benzonatate benzthiazide, benztropine mesylate, betaine, betamethasone, betaxolol, betanecol chloride, biotin, biperiden, bisacodyl, bismuth, botulism antitoxin, bromocriptine mesylate, bromodiphenhydramine hydrochloride, bumetanide, bupivacaine, busulfan butabarbital sodium, butalbital, combinations of butalbital, caffeine and aspirin and codeine, beta-carotene, calcifediol, calcium carbonate, calcium citrate, calcium salts, candidin, captopril, carbachol, carbamazepine, carbenicillin indanyl sodium, carbidopa, carbinoxamine maleate, carboprost tromethamine, carboxymethyl cellulose, carisoprodol, casanthranol, cascara, castor oil, cefaclor, cefadroxil, cefamandole nafate, cefazolin, cefixime, cefoperazone, cefotaxime, cefprozil, ceftazidime, cefuroxime axetil, cephalixin, cephradine, chlorambucil, chloramphenicol, chlordiazepoxide, chloroquine phosphate, chlormadinone acetate, chlorothiazide, chlorpheniramine maleate, chloroxylonol, chlorpromazine, chlorpropamide, chlorprothixene, chlorprothixene, chlortetracycline bisulfate, chlortetracycline hydrochloride, chlorthalidone, chlorzoxazone, cholecalciferol, cholera vaccine, chromic chloride, chymotrypsin, cimetidine, cinoxazin, cinoxate, ciprofloxacin, cisplatin, clarithromycin, clavulanate potassium, clemastine fumarate, clidinium bromide, clindamycin hydrochloride, -palmitate and -phosphate, clioquinol, clofazimine, clofibrate, clomiphene citrate, clonazepam, cinnarizine, clonidine hydrochloride, clorsulon, clotrimazole, cloxacillin sodium, cyanocobalamin, cocaine, coccidioidin, cod liver oil, codeine, colchicine, colestipol, corticotropin, corisone acetate, cyclacillin, cyclizine hydrochloride,

cyclobenzaprine hydrochloride, cyclophosphamide, cycloserine, cyclosporine, cyproheptadine hydrochloride, cysteine hydrochloride, danazol, dapsone, dehydrocholic acid, demeclocycline, desipramine, desoximetasone, desoxycorticosterone acetate, dexamethasone, dexchlorpheniramine maleate, dexpanthenol, dextroamphetamine, dextromethorphan, diazepam, diazoxide, dibucaine, dichlorphenamide, dicloxacillin sodium, dicyclomine, dienestrol, diethylpropion hydrochlorid, diethylstilbestrol, diflunisal, digitalis, dicoumarol, digitoxin, digoxin, dihydroergotamine, dihydrostreptomycin, dihydrotachysterol, dihydroxyaluminium amino acetate, dihydroxyaluminium sodium carbonate, diltiazem hydrochloride, dimenhydrinate, dimercaprol, diphenhydramine hydrochloride, diphenoxylate hydrochloride, diphteria antitoxin, dipyridamole, disopyramide phosphate, disulfiram, dobutamine hydrochloride, docusate calcium, docusate sodium, dopamine hydrochloride, doxepin hydrochloride, doxycycline, doxycycline hyclate, doxylamine succinate, dronabinol, droperidol, drotaverine, dydrogesterone, dyphylline, guaifenesin, enalapril maleate, analaprilat, ephedrine, epinephrine, equilin, ergocalciferol, ergoloid mesylates, ergonovine maleate, ergotamine tartrate, erythryl tetranitrate, erythromycin, estradiol, estriol, estrogene, estrone, estropipate, ethcryninc acid, ethambutol hydrochloride, ethchlorvynol, ethinyl estradiol, ethionamide, ethopropazine hydrochloride, ethotoin, ethynodiol diacetate, etidronate disodium, etoposide, eugenol, famotidine, fenoprofen, ferrous fumarate, ferrous gluconate, ferrous sulfate, flucytosine, fludrocortisone acetate, flunisolide, fluocinolone acetonide, fluocinonide, fluorescein sodium, fluorometolone, fluorouracil, fluoxymesterone, fluphenazine, flurandrenolide, flurazepam, flurbiprofen, folic acid, furazolidone, flunitrazepam, furosemide, gemfibrozil, gentamicin, gentian violet, glutarate, glutethimide, glycopyrrolate, chorionic gonadotropin, gramicidin, griseofulvin, guaifenesin, guanabenz, guanadrel sulfate, halazone, haloperidol, haloprogin, halothane, heparin calcium, hepatitis virus vaccine, hetacillin potassium, hexylresorcinol, histamine phosphate, histidine, homatropine, histoplasmin, hydralazine hydrochloride, hydrochlorothiazide, hydrocodone bitartrate, hydrocortisone, hexobarbital, hydroflumethiazide, hydromorphone hydrochloride, hydroquinone, hydroxocobalamin, hydroxyamphetamine, hydroxychloroquine sulfate, hydroxyprogesterone caproate, hydroxyurea, hydroxine hydrochloride, hydroxine pamoate, hyoscyamine, hyoscyamine sulfate, ibuprofen, ifosfamide, imipramide, imipramide hydrochloride, indapamide, indomethacin, insulin, inulin, iocetamid, iodoquinol, iohexol, iopamidol, ipecac, ipodate calcium, ipodate sodium, isocarboxacid, isoetharine hydrochloride, isoflurane, isoniaacid, isopropamide iodine, isoproterenol hydrochloride, isosorbide dinitrate, isotretenoin, isoxsuprine hydrochloride, kanamycin sulfate, ketoprofen, ketoconazole, labetalol hydrochloride, lanolin, leucine, leucovorin calcium, levamisole hydrochloride, levocamithine, levodopa, levonorgestrel, levorphanol tartrate, levothyroxine sodium, lidocaine, lincomycin hydrochloride, lindane, liothyronine sodium, liotrix, lisinopril, lithium carbonate, loperamide hydrochloride, loracarbef, lonetil, lorazepam, lovastatin, loxapine, lysine, mafenide acetate, magaldrt, magnesium carbonate, magnesiumchloride, magnesium gluconate, magnesium oxide, other magnesium salts, malathion, manganese salts, manganese, maprotiline hydrochloride, mazindol, measles virus vaccine, mebendazole, mebrofenin, mecamlamine hydrochloride, meclizine hydrochloride, meclocycline, meclofenamate sodium, medroxyprogesterone acetate, mefenamic acid, megestrol acetate, meglumine, melphalan, menadiol sodium diphosphate, menadione, menotropine, meperidine, mephenytoin, mephobarbital, meprednisone,

meprobamate, mercaptopurine, mesoridazine besylate, mestranol, metaproterenol sulfate, metaraminol bitartrate, methacycline hydrochloride, methadone hydrochloride, methamphetamine hydrochloride, methazolamide, methdilazine, methenamine, methicillin sodium, methimazole, methionine, methocarbamol, methotrexate, methoxsalen, methoxyflurane, methsuximide, methyclothiazide, methylbenzethonium chloride, methyl dopa, methylergonovine maleate, methylphenidate hydrochloride, methylprednisolone, methyltestosterone, methysergide maleate, metoclopramide, metolazone, meoprolol tartrate, metronidazole, metyrapone, metyrosine, mexiletine hydrochloride, mexiletine hydrochloride, miconazole, minocycline hydrochloride, minoxidil, mitomycin, mitotane, molindone hydrochloride, monobenzene, morphine sulfate, mupirocin, medazepam, mefruside, methandrostenolone, methylsulfadiazine, nadolol, nafcillin, nafcillin sodium, nalidixic acid, nalorphine, naloxone, nandrolone decanoate, nandrolone phenpropionate, naproxen, natamycin, neomycin, neomycin sulfate, neostimine bromide, niacin, nitrofurantoin, nalidixic acid, nifedipine, nitrazepam, nitrofurantoin, nitroglycerine, nitromerson, nizatidine, nonoxynol 9, norethindrone, norethindrone acetate, norfloxacin, norgestrel, nortriptyline hydrochloride, noscapine, novobiocin sodium, nystatin, opium, oxacillin sodium, oxamniquine, oxandrolone, oxazepam, oxprenolol hydrochloride, oxtriphylline, oxybenzone, oxybutynin chloride, oxycodone hydrochloride, oxycodone, oxymetazoline hydrochloride, oxymetholone, oxymorphone hydrochloride, oxyphenbutazone, oxytetracycline, padimate, panreatin, pancrelipase, papain, panthenol, papaverin hydrochloride, parachlorophenol, paramethasone acetate, paregoric, paromomycin sulfate, penicillamine, penicillin, penicillin derivatives, pentaerythritol tetranitrate, pentazocine, pentazocine hydrochloride, pentazocine salts, pentobarbital sodium, perphenazine, pertussis, phenacetamide, phenazopyridine hydrochloride, phendimetrazine tartrate, phenelzine sulfate, phenmetrazine hydrochloride, phenobarbital, phenophtalein, phenoxybenzamine hydrochloride, phentermine hydrochloride, phenylalanine, phenylbutazone, phenylephrine hydrochloride, phenylpropanolamine hydrochloride, physostigmine, phytonadione, pilocarpine, pimozide, pindolol, piperazine, piroxicam, plicamycin, poliovirus vaccine inactivated, polycarbophil, polymycin b sulfate, polythiazide, potassium chloride, potassium citrate, potassium cluconate, potassium iodine, potassium sodium tartrate, povidone iodine, pralidoxime chloride, pramoxine hydrochloride, pramezam, prazepam, praziquantel, prazosin hydrochloride, prazosin hydrochloride, prednisolone, prilocaine, primaquine, primidone, probenecid, probucol, procainamide hydrochloride, procaine hydrochloride, procarbazine hydrochloride, prochlorperazine, prochlorperazine maleate, procyclidine hydrochloride, progesterone, proline, promazine, promazine hydrochloride, promazine, promethazine, promethazine hydrochloride, propafenone hydrochloride, propantheline, proparacaine hydrochloride, propoxycaine hydrochloride, propoxyphene hydrochloride, propoxyphene napsylate, propanolol hydrochloride, propylidone, propylthiouracil, propylthiouracil, protriptyline hydrochloride, pseudoephedrine hydrochloride, pumice, pyrantel pamoate, pyrazinamide, pyrethrum extract, pyridostigmine bromide, pyridoxine hydrochloride, pyrilamine maleate, pyrimethamine, pyroxylin, pyrvinium pamoate, phenacetin, phenytoin, prednisone, uinidine gluconate, quinidine sulfate, rabies vaccine, racepinephrine, ranitidine, rauwolfia serpentina, resorcinol, ribavirin, riboflavin, rifampin, ritodrine, rubella virus vaccine, saccharin, saccharin sodium, salicylamide, salicylic acid, salsalata, scopolamine, secobarbital sodium, selenius acid, selenium sulfate, sennaserine, simethicone, sodium ascorbate, sodium bicarbonate, sodium fluoride, sodium gluconate, sodium

iodide, sodium lactate, sodium nitrite, sodium ditroprusside, sodium salicylate, spironolactone, stannozolol, streptomycin, sucralfate, sulfacetamide, sulfadiazine, reserpine, sulfadioxine, sulfamerazine, sulfamethazine, sulfamethizole, sulfamethoxazole, sulfamethoxydiazine, sulfapyridin, sulfasalazine, sulfaperin, sulfathiazole, sulfisoxazole, sulfinpyrazone, sulindac, suprofen, stilains, tamoxifen citrate, temacepam, terbutaline sulfate, terfenadine, terpin, testolacton, testosterone, tolazamide, tolbutamide, tetracaine, tetracycline, tetrahydrocycline, theophylline, thiabendazole, thiamine hydrochloride, thiamin, thiamylal, thiethylperazine thimerosal, thioguanine, thioridazine hydrochloride, thistrepton, thiotepa, thiothixene, threonine, thyroid, ticarcillin, timolol, tioconazole, titaniumdioxide, tolazamide, tolbutamide, tolmetin, tolnaftate, trazodone hydrochloride, tretinoin, triacetin, triamcinolone, triamterene, triazolam, trichorfon, trichlormethiazide, trientine hydrochloride, trifluoperazine hydrochloride, triflupromazine, trihexyphenidyl hydrochloride, trimepazine tartrate, trimethadione, trimethobenzamide hydrochloride, trimethoprim, trioxsalen, tripelennamine, triprolidine, trisulfapyrimidine, tropicamide, trypsin, tryptohan, tuberculin, tyloxapol, tyropanoate sodium, tyrosine, tyrothricin, thyrothricin bethamethasone, thiotic acid, sotalol, salbutamol, norfenefrine, silymarin, dihydroergotamine, buflomedil, etofibrate, indometacin, urea, valine, valproic acid, vancomycin hydrochloride, vasopressin, verapamil, vidarabine, vinblastine, vincristine, vitamins, warfarin, yellow fever vaccine, zinc acetate, zinc carbonate, zinc chloride, zinc gluconate, beta acetyl digoxin, piroxicam, haloperidol, ISMN, amitriptylin, diclofenac, nifedipine, verapamil, pyritinol, nitrendipin, doxycycline, bromhexine, methylprdnisolone, clonidine, fenofibrate, allopurinol, pirenepine, levothyroxin, tamoxifen, metildigoxin, o-(beta-hydroxyethyl)-rutoside, propicillin, aciclovir mononitrate, paracetamol, naftidrofuryl, pentoxifylline, propafenone, acebutolol, L-thyroxin, tramadol, bromocriptine, loperamide, ketotifen, fenoterol, cadobelisate, propanolol, enalaprilhydrogen maleate, bezafibrate, ISDN, gallopamil, xantinol nicotinate, digitoxin, flunitrazepam, bencyclane, dexapanthenol, pindolol, lorazepam, diltiazem, piracetam, phenoxymethylpenicillin, furosemide, bromazepam, flunarizin, erythromycin, metoclopramide, acemetacin, ranitidin, biperiden, metamizole, doxepin, dipotassium chlorazepate, tetrazepam, estramustine phosphate, terbutaline, captopril, maprotiline, prazosin, atenolol, glibenclamide, cefaclor, etilfrine, cimetidine, theophylline, hydromorphone, ibuprofen, primidone, clobazam, oxaceprol, medroxyprogesterone, flecainid, pyridoxal 5 phosphate glutamine, hymechromone, etofylline clofibrate, vincamine, cinnarizine, diazepam, ketoprofen, flupentixol, molsimine, glibornuride, dimetinden, melperone, soquinolol, dihydrocodeine, clomethiazole, clemastine, glisoxepide, kallidinogenase, oxyfedrine, baclofen, carboxymethylcysteine, thioridazine, betahistine, L-tryptophan, murtol, bromelaine, prenylamine, salazosulfapyridine, astemizol, sulpiride, benzerazide, dibenzepine, acetylsalicylic acid, miconazol, nystatin, ketoconazole, sodium picosulfate, coltyramine, gemfibrocil, rifampicin, fluocortolone, mexiletin, amoxicillin, terfenadrin, mucopolysaccharide polysulfade, triazolam, mianserin, tiaprofenic acid, amezinium metilsulfate, mefloquine, probucol, quinidine, carbamazepine, L-aspartate, penbutolol, piretanide, aescin amitriptyline, cyproterone, sodium valproinate, mebeverine, bisacodyl, 5-aminosalicylic acid, dihydralazine, magaldrate, phenprocoumon, amantadine, naproxen, carteolol, famotidine, methyl dopa, aurano fine, estriol, nadolol, levomepromazine, doxorubicin,

medofenoxate, azathioprine, flutamide, norfloxacin, fendiline, prajmalium bitartrate, lipid derivatives of phosphonates, amphiphilic polymers, adenosine derivatives, sulfated tannins, monoclonal antibodies, and metal complexes of water soluble texathrin.

Other Reference Publication - OREF (1):

Per Artusson et al., "Characterization of Polyacryl Starch Microparticles as Carriers for Proteins and Drugs," Journal of Pharmaceutical Science, vol. 73, No. 11, pps. 1507-1513 (Nov. 1984).

Other Reference Publication - OREF (2):

Lennart Randen et al., "Coprecipitation of Enzymes with Water Soluble Starch--An Alternative to Freeze-drying," J. Pharm. Pharmacol., vol. 40, pps. 763-766 (1988):

Other Reference Publication - OREF (3):

Shigeaki Maruo et al., "Effects of Moranoline, 4-O-.alpha.-D-Glucopyranosylmoranoline and Their N-Substituted Derivatives on Thermostability of Cyclodextrin Glycosyltransferase, Glucoamylase, and .beta.-Amylase," Biosci. Biotech. Biochem., vol. 57, No. 8, pps. 1294-1298, (1993).

Other Reference Publication - OREF (4):

Wendell Q. Sun et al., "Protein stability in the amorphous carbohydrate matrix: relevance to anhydrobiosis," Biochimica et Biophysica Acta, vol. 1425, pps. 245-254 (1998).

Other Reference Publication - OREF (5):

Colonna et al., "Extrusion Cooking of Starch & Starchy Products," Extrusion Cooking, C. Mercier, et al. AACC, St. Paul, MN (1989), pps. 247-319.

Other Reference Publication - OREF (6):

Meuser et al., "A Systems Analytical Approach To Extrusion," Food Extrusion Science & Technology, ed. J. Kokini, Dekker Publ. (1992), pps. 619-630.

US-PAT-NO: 6194457

DOCUMENT-IDENTIFIER: US 6194457 B1

\*\*See image for Certificate of Correction\*\*

TITLE: Liquid eye drop composition

DATE-ISSUED: February 27, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Braswell; A. Glenn	Marine del Rey	GA	90292	N/A
Absher; Kenneth J.	Carson City	NV	89703	N/A
Duarte; Alex	Nevada City	CA	95959	N/A

APPL-NO: 09/ 015755

DATE FILED: January 29, 1998

PARENT-CASE:

This nonprovisional application claims the benefit of U.S. Provisional Application No. 06/036,516, filed Jan. 29, 1997.

US-CL-CURRENT: 514/547, 514/561, 514/562, 514/912

ABSTRACT:

A composition that is used as an eye treatment contains reduced glutathione, vitamin A and vitamin E, as well as one or more of zinc sulfate, boric acid and potassium as buffering agents. The composition also may contain a lubricant and a preservative. The composition is a sterile isotonic solution. The composition is used in a method of treating eyes for the alleviation of irritations and/or dryness, as well as for the prevention and treatment of cataracts.

20 Claims, 0 Drawing figures

Exemplary Claim Number: 1

----- KWIC -----

Brief Summary Text - BSTX (7):

Light entering the eye permits the generation of free radicals within the lens, in particular the superoxide radical  $O_{2}^{\cdot -}$ , which in turn can degenerate into other free radicals such as hydrogen peroxide and hydroxide radicals. These free radicals act to oxidize the proteins of the lens. Oxidation of the proteins is known to be a major factor leading to the onset of

cataracts, which is a loss of transparency of the lens. See, for example, Varma, "Scientific Basis for Medical Therapy of Cataracts by Antioxidants", *Am. S. Clin. Nutr.*, vol. 53, pps. 335S-345S (1991).

Brief Summary Text - BSTX (8):

Accordingly, the lens of the eye has an antioxidant defense system to respond to an oxidative stress and maintain the integrity of the lens. Various studies have shown that the antioxidant defense system includes the enzymes glutathione peroxidase, catalase and superoxide dismutase, and the antioxidants vitamin A (ascorbic acid), vitamin E (.alpha.-tocopherol) and .beta.-~~carotene~~. See, for example, Kamei, "Glutathione Levels of the Human Crystalline Lens in Aging", *Biol. Pharm. Bull.*, vol. 16, no. 9, pps. 870-875 (1993); Fletcher et al., "Glutathione and Aging: Ideas and Evidence", *The Lancet*, vol. 344, pps. 1379-1380 (1994); and Jacques et al., "Antioxidant Status in Persons With and Without Senile Cataracts", *Arch. Ophthalmol.*, vol. 106, pps. 337-340 (1988).

Brief Summary Text - BSTX (9):

The role of each of the above materials in protecting the lens against degradation by oxidation has also been widely studied. Most studies have focused upon dietary supplementation of the materials to preserve the antioxidant defense system of the lens during aging, thus preventing or slowing the onset of cataracts. See, for example, Robertson et al., "Vitamin E Intake and Risk of Cataracts in Humans", *Annals New York Academy of Sciences*, pps. 372-382; "Protective Role of Vitamin E in Cataract Development", *Vitamin E Research Information Service* (1990); Devamanoharan et al., "Prevention of Selenite Cataract by Vitamin C", *Exp. Eye Res.*, vol. 52, pps. 563-568 (1991); and Jacques et al., "Epidemiologic Evidence of a Role for the Antioxidant Vitamins and Carotenoids in Cataract Prevention", *Am. J. Clin. Nutr.*, vol. 53, pps. 352S-355S (1991). See also U.S. Pat. No. 5,075,116 to LaHaye et al.

Brief Summary Text - BSTX (10):

Studies have also confirmed that the materials vitamin A, vitamin E and glutathione have a close interaction in regenerating one another following oxidation of one or more of these molecules. See, for example, Stoyanovsky et al., "Endogenous Ascorbate Regenerates Vitamin E in the Retina Directly and in Combination With Exogenous Dihydrolipoic Acid", *Current Eye Research* (1994); and Winkler et al., "The Redox Couple Between Glutathione and Ascorbic Acid: A Chemical and Physiological Perspective", *Free Radical Biology & Medicine*, vol. 17, no. 4, pps. 333-349 (1994).

Brief Summary Text - BSTX (11):

A role has also been reported for zinc and copper in maintenance of retinal metabolism. See Hirayama, "Histochemical Localization of Zinc and Copper in Rat Ocular Tissues", *Acta Histochem.*, vol. 89, pps. 107-111 (1990). Zinc has been cited as a cofactor for several antioxidant systems present in the retinal pigment epithelium. See Newsome et al., "Zinc Uptake by Primate Retinal Pigment Epithelium and Choroid", *Current Eye Research*, vol. 11, no. 3, pps. 213-217 (1992).

Brief Summary Text - BSTX (27):

The eye treatment composition of the invention is a solution preferably having a vehicle of water, preferably deionized water, or mixtures of water and water-miscible solvents such as, for example, lower alkanols or arylalkanols, phosphate buffer vehicle systems, isotonic vehicles such as boric acid, sodium chloride, sodium citrate, sodium acetate and the like, vegetable oils, polyalkylene glycols, and petroleum based jelly, as well as aqueous solutions containing ethyl cellulose, carboxymethyl cellulose and derivatives thereof, hydroxypropylmethyl cellulose, hydroxyethyl cellulose, carbopol, polyvinyl alcohol, polyvinyl pyrrolidone, isopropyl myristate and other conventionally-employed non-toxic, pharmaceutically acceptable organic and inorganic carriers. The aqueous-based vehicle comprises the balance of the eye drop composition.



US-PAT-NO: 6130321

DOCUMENT-IDENTIFIER: US 6130321 A

TITLE: High tap density chitosan, and methods of production

DATE-ISSUED: October 10, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Johnson; Edwin Lee	Issaquah	WA	N/A	N/A
Nichols; Everett Junior	Edmonds	WA	N/A	N/A

APPL-NO: 09/ 114023

DATE FILED: July 10, 1998

US-CL-CURRENT: 536/20

ABSTRACT:

The present invention provides novel methods of producing chitosan having a tap density of at least about 0.4 g/ml. In one aspect of the present invention, chitosan is selected having an average molecular mass of from about one thousand Daltons to about two million Daltons; a particle size that is smaller than 20 mesh; a viscosity of at least about 1 cps, and a percentage of deacetylation of from about 65% to about 98%. A measured amount of the selected chitosan is then mixed with an amount of water that is from about two to about ten times the weight of the chitosan, and an amount of an acid that is at least about 0.1% of the weight of the chitosan. The acid is preferably an organic acid. The mixture of chitosan, water and acid is then mixed to a smooth paste, dried to a moisture content of from 0% moisture to about 20% moisture, and the particle size is preferably reduced to smaller than 20 mesh. In another aspect of the invention, chitosan is provided having a tap density of at least about 0.4 g/ml and the ability to freely flow through an orifice having a circular cross section having a diameter of about 4 mm. The chitosan of the present invention is relatively odorless.

34 Claims, 4 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 4

----- KWIC -----

Brief Summary Text - BSTX (6):

With respect to the use of chitosan as a dietary supplement, chitosan is

often used to reduce the blood serum level of cholesterol, and to promote weight loss by impeding dietary fat absorption in the gastrointestinal tract. Chitosan can be encapsulated or tabletized either alone or in combination with other ingredients including vitamins C, E, B6, .beta.-carotene, folic acid, and a variety of binders. For the benefit of those individuals who have difficulty swallowing tablets or capsules, chitosan can be added to baked goods, such as crackers, cookies and cakes, and to beverages. Again, a high density preparation of chitosan is desirable because, for example, a smaller volume of high density chitosan need be consumed, compared to standard, lower density chitosan, in order to deliver the same dose of chitosan. Thus, for example, a person need consume fewer tablets or capsules of high density chitosan compared to standard preparations of lower density chitosan.

Claims Text - CLTX (41):

33. Chitosan of claim 23 wherein said chitosan is selected from the group consisting of chitosan succinate, chitosan adipate, chitosan chloride, chitosan glutamate, chitosan lactate, chitosan aspartate, chitosan acetate, chitosan pyruvate, and chitosan malate.

Claims Text - CLTX (42):

34. Chitosan of claim 27 wherein said chitosan is selected from the group consisting of chitosan succinate, chitosan adipate, chitosan chloride, chitosan glutamate, chitosan lactate, chitosan aspartate, chitosan acetate, chitosan pyruvate, and chitosan malate.

Other Reference Publication - OREF (1):

T. Yui et al., "Molecular and Crystal Structure of the Anhydrous Form of Chitosan", *Macromolecules*, vol. 27, pps. 7601-7605, (Dec. 1994).

Other Reference Publication - OREF (2):

G. G. Allan, M. Peyron, "Molecular weight manipulation of chitosan I: kinetics of depolymerization by nitruos acid", *Carbohydrate Research*, vol. 277, pps. 257-272 (1995) month not available.

Other Reference Publication - OREF (3):

J. Li, J.F. Revol and R.H. Marchessault, Effect of Degree of Deacetylation of Chitin on the Properties of Chitin Crystallites, John Wiley & Sons, Inc. ccc 0021-8995/97/020373-08., pps. 373-380 (1997) month not available.

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 15:29:16 ON 17 JUN 2003

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COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
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FULL ESTIMATED COST

FILES 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS, ESBIODBASE, BIOTECHNO, WPIDS' ENTERED AT 15:48:52 ON 17 JUN 2003  
ALL COPYRIGHTS AND RESTRICTIONS APPLY. SEE HELP USAGETERMS FOR DETAILS.

11 FILES IN THE FILE LIST

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FILE 'MEDLINE'

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FILE 'SCISEARCH'

L2 35 GLNAP?

FILE 'LIFESCI'

L3 49 GLNAP?

FILE 'BIOTECHDS'

L4 5 GLNAP?

FILE 'BIOSIS'

L5 56 GLNAP?

FILE 'EMBASE'

L6 45 GLNAP?

FILE 'HCAPLUS'

L7 62 GLNAP?

FILE 'NTIS'

L8 0 GLNAP?

FILE 'ESBIODBASE'

L9 22 GLNAP?

FILE 'BIOTECHNO'

L10 43 GLNAP?

FILE 'WPIDS'

L11 2 GLNAP?

TOTAL FOR ALL FILES

L12 373 GLNAP?

=> s acetyl phosphate or acetylphosphate or acetate

FILE 'MEDLINE'

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123587 PHOSPHATE

324 ACETYL PHOSPHATE

(ACETYL(W) PHOSPHATE)

71 ACETYLPHOSPHATE

85997 ACETATE

L13 86292 ACETYL PHOSPHATE OR ACETYLPHOSPHATE OR ACETATE

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127161 PHOSPHATE  
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23165 ACETATE  
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11055 ACETATE  
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186290 PHOSPHATE  
422 ACETYL PHOSPHATE  
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78 ACETYLPHOSPHATE  
112682 ACETATE  
L17 113043 ACETYL PHOSPHATE OR ACETYLPHOSPHATE OR ACETATE

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151764 "PHOSPHATE"  
265 ACETYL PHOSPHATE  
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40 ACETYLPHOSPHATE  
99814 ACETATE  
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236 ACETYLPHOSPHATE  
449406 ACETATE  
L19 450162 ACETYL PHOSPHATE OR ACETYLPHOSPHATE OR ACETATE

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35348 PHOSPHATE

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 48786 PHOSPHATE  
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 (ACETYL(W) PHOSPHATE)  
 28 ACETYLPHOSPHATE  
 28164 ACETATE  
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 79708 PHOSPHATE  
 31 ACETYL PHOSPHATE  
 (ACETYL(W) PHOSPHATE)  
 17 ACETYLPHOSPHATE  
 109139 ACETATE  
 L23 109165 ACETYL PHOSPHATE OR ACETYLPHOSPHATE OR ACETATE  
  
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 L27 58126 PROMOTER?  
  
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 L28 27161 PROMOTER?  
  
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 L29 110649 PROMOTER?  
  
 FILE 'EMBASE'  
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 FILE 'NTIS'  
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 L34 71268 PROMOTER?  
  
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 L35 28369 PROMOTER?  
  
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    617895 REGULAT?
    612120 ACTIVAT?
    177205 MODULAT?
    26673 L25(8A)(INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)
L37      32 L1 AND (L13 OR L25(8A)(INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT
        ?))

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    662571 ACTIVAT?
    254318 MODULAT?
    27369 L26(8A)(INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)
L38      24 L2 AND (L14 OR L26(8A)(INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT
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    216162 REGULAT?
    196755 ACTIVAT?
    65773 MODULAT?
    19111 L27(8A)(INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)
L39      30 L3 AND (L15 OR L27(8A)(INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT
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    34401 INDUC?
    21620 REGULAT?
    20686 ACTIVAT?
    8840 MODULAT?
    5161 L28(8A)(INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)
L40      4 L4 AND (L16 OR L28(8A)(INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT
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    677816 REGULAT?
    630593 ACTIVAT?
    208034 MODULAT?
    33110 L29(8A)(INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)
L41      37 L5 AND (L17 OR L29(8A)(INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT
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    534507 ACTIVAT?
    170139 MODULAT?
    25027 L30(8A)(INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)
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    766708 REGULAT?
    1054351 ACTIVAT?
    264423 MODULAT?
    42072 L31(8A)(INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)
L43      45 L7 AND (L19 OR L31(8A)(INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT
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80764 REGULAT?  
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20991 MODULAT?

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81816 MODULAT?

17806 L33(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)  
L45 16 L9 AND (L21 OR L33(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT  
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250585 REGULAT?  
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53769 MODULAT?

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L46 27 L10 AND (L22 OR L34(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULA  
T?))

FILE 'WPIDS'

218634 INDUC?  
335753 REGULAT?  
219138 ACTIVAT?  
137137 MODULAT?

3806 L35(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)  
L47 2 L11 AND (L23 OR L35(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULA  
T?))

TOTAL FOR ALL FILES

L48 246 L12 AND (L24 OR L36(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULA  
T?))

=> s l24(8a)l36(8a)(induc? or regulat? or activat? or modulat?)

FILE 'MEDLINE'

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617895 REGULAT?  
612120 ACTIVAT?  
177205 MODULAT?

L49 571 L13(8A)L25(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)

FILE 'SCISEARCH'

1280733 INDUC?  
531767 REGULAT?  
662571 ACTIVAT?  
254318 MODULAT?

L50 373 L14(8A)L26(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)

FILE 'LIFESCI'

365306 INDUC?  
216162 REGULAT?  
196755 ACTIVAT?  
65773 MODULAT?

L51 238 L15(8A)L27(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)

FILE 'BIOTECHDS'

34401 INDUC?

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        21620 REGULAT?
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L52      7 L16(8A)L28(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)

FILE 'BIOSIS'
        1312404 INDUC?
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        630593 ACTIVAT?
        208034 MODULAT?
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FILE 'EMBASE'
        1073075 INDUC?
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        534507 ACTIVAT?
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FILE 'NTIS'
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        80764 REGULAT?
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        250585 REGULAT?
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        53769 MODULAT?
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FILE 'WPIDS'
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        335753 REGULAT?
        219138 ACTIVAT?
        137137 MODULAT?
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TOTAL FOR ALL FILES
L60      3588 L24(8A) L36(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)

=> s l60 not ((phorbol or tetradecanoylphorbol) (2a)acetate)
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        26725 TETRADECANOYLPORBOL
        85997 ACETATE
        30437 (PHORBOL OR TETRADECANOYLPORBOL) (2A)ACETATE
L61      35 L49 NOT ((PHORBOL OR TETRADECANOYLPORBOL) (2A)ACETATE)

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FILE 'SCISEARCH'

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4491 TETRADECANOYLPHORBOL  
83662 ACETATE  
11169 (PHORBOL OR TETRADECANOYLPHORBOL) (2A)ACETATE  
L62 84 L50 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A)ACETATE)

FILE 'LIFESCI'

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2294 TETRADECANOYLPHORBOL  
23165 ACETATE  
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FILE 'BIOTECHDS'

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47 TETRADECANOYLPHORBOL  
11055 ACETATE  
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FILE 'BIOSIS'

37478 PHORBOL  
9328 TETRADECANOYLPHORBOL  
112682 ACETATE  
21297 (PHORBOL OR TETRADECANOYLPHORBOL) (2A)ACETATE  
L65 112 L53 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A)ACETATE)

FILE 'EMBASE'

36797 PHORBOL  
5982 TETRADECANOYLPHORBOL  
99814 ACETATE  
24891 (PHORBOL OR TETRADECANOYLPHORBOL) (2A)ACETATE  
L66 45 L54 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A)ACETATE)

FILE 'HCAPLUS'

30927 PHORBOL  
6318 TETRADECANOYLPHORBOL  
449406 ACETATE  
15765 (PHORBOL OR TETRADECANOYLPHORBOL) (2A)ACETATE  
L67 134 L55 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A)ACETATE)

FILE 'NTIS'

194 PHORBOL  
29 TETRADECANOYLPHORBOL  
3039 ACETATE  
80 (PHORBOL OR TETRADECANOYLPHORBOL) (2A)ACETATE  
L68 0 L56 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A)ACETATE)

FILE 'ESBIOBASE'

10955 PHORBOL  
1968 TETRADECANOYLPHORBOL  
22040 ACETATE  
4576 (PHORBOL OR TETRADECANOYLPHORBOL) (2A)ACETATE  
L69 55 L57 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A)ACETATE)

FILE 'BIOTECHNO'

18056 PHORBOL  
3163 TETRADECANOYLPHORBOL  
28164 ACETATE  
11969 (PHORBOL OR TETRADECANOYLPHORBOL) (2A)ACETATE  
L70 37 L58 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A)ACETATE)

FILE 'WPIDS'

288 PHORBOL  
40 TETRADECANOYLPHORBOL  
109139 ACETATE  
137 (PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE  
L71 4 L59 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE)

TOTAL FOR ALL FILES

L72 556 L60 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE)

=> s pps or phosphoenol pyruvate synthase#

FILE 'MEDLINE'

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23415 PYRUVATE  
71030 SYNTHASE#  
0 PHOSPHOENOL PYRUVATE SYNTHASE#  
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L73 2102 PPS OR PHOSPHOENOL PYRUVATE SYNTHASE#

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FILE 'LIFESCI'

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5779 "PYRUVATE"  
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FILE 'BIOTECHDS'

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104 PHOSPHOENOL  
1784 PYRUVATE  
4448 SYNTHASE#  
21 PHOSPHOENOL PYRUVATE SYNTHASE#  
(PHOSPHOENOL (W) PYRUVATE (W) SYNTHASE#)  
L76 108 PPS OR PHOSPHOENOL PYRUVATE SYNTHASE#

FILE 'BIOSIS'

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3651 PHOSPHOENOL  
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11 PHOSPHOENOL PYRUVATE SYNTHASE#  
(PHOSPHOENOL (W) PYRUVATE (W) SYNTHASE#)  
L77 1104 PPS OR PHOSPHOENOL PYRUVATE SYNTHASE#

FILE 'EMBASE'

1381 PPS  
173 "PHOSPHOENOL"  
19215 "PYRUVATE"  
69481 SYNTHASE#  
0 PHOSPHOENOL PYRUVATE SYNTHASE#  
( "PHOSPHOENOL" (W) "PYRUVATE" (W) SYNTHASE#)  
L78 1381 PPS OR PHOSPHOENOL PYRUVATE SYNTHASE#

```

FILE 'HCAPLUS'
    2657 PPS
    676 PHOSPHOENOL
    46724 PYRUVATE
    72314 SYNTHASE#
    7 PHOSPHOENOL PYRUVATE SYNTHASE#
      (PHOSPHOENOL(W) PYRUVATE(W) SYNTHASE#)
L79      2662 PPS OR PHOSPHOENOL PYRUVATE SYNTHASE#

FILE 'NTIS'
    689 PPS
    5 PHOSPHOENOL
    304 PYRUVATE
    202 SYNTHASE#
    0 PHOSPHOENOL PYRUVATE SYNTHASE#
      (PHOSPHOENOL(W) PYRUVATE(W) SYNTHASE#)
L80      689 PPS OR PHOSPHOENOL PYRUVATE SYNTHASE#

FILE 'ESBIOBASE'
    419 PPS
    72 PHOSPHOENOL
    5427 PYRUVATE
    31769 SYNTHASE#
    0 PHOSPHOENOL PYRUVATE SYNTHASE#
      (PHOSPHOENOL(W) PYRUVATE(W) SYNTHASE#)
L81      419 PPS OR PHOSPHOENOL PYRUVATE SYNTHASE#

FILE 'BIOTECHNO'
    231 PPS
    77 PHOSPHOENOL
    6261 PYRUVATE
    27132 SYNTHASE#
    0 PHOSPHOENOL PYRUVATE SYNTHASE#
      (PHOSPHOENOL(W) PYRUVATE(W) SYNTHASE#)
L82      231 PPS OR PHOSPHOENOL PYRUVATE SYNTHASE#

FILE 'WPIDS'
    1273 PPS
    166 PHOSPHOENOL
    1620 PYRUVATE
    3209 SYNTHASE#
    24 PHOSPHOENOL PYRUVATE SYNTHASE#
      (PHOSPHOENOL(W) PYRUVATE(W) SYNTHASE#)
L83      1275 PPS OR PHOSPHOENOL PYRUVATE SYNTHASE#

TOTAL FOR ALL FILES
L84      12257 PPS OR PHOSPHOENOL PYRUVATE SYNTHASE#

=> s 184(5a)gene/q
FILE 'MEDLINE'
L85      39 L73(5A)GENE/Q

FILE 'SCISEARCH'
L86      40 L74(5A)GENE/Q

FILE 'LIFESCI'
L87      27 L75(5A)GENE/Q

FILE 'BIOTECHDS'
L88      37 L76(5A)GENE/Q

FILE 'BIOSIS'
L89      54 L77(5A)GENE/Q

```

```

FILE 'EMBASE'
L90          36 L78 (5A) GENE/Q

FILE 'HCAPLUS'
L91          111 L79 (5A) GENE/Q

FILE 'NTIS'
L92          1 L80 (5A) GENE/Q

FILE 'ESBIOBASE'
L93          27 L81 (5A) GENE/Q

FILE 'BIOTECHNO'
L94          28 L82 (5A) GENE/Q

FILE 'WPIDS'
L95          43 L83 (5A) GENE/Q

TOTAL FOR ALL FILES
L96          443 L84 (5A) GENE/Q

=> s phosphoenolpyruvate synthase#
FILE 'MEDLINE'
          6307 PHOSPHOENOLPYRUVATE
          71030 SYNTHASE#
L97          27 PHOSPHOENOLPYRUVATE SYNTHASE#
          (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)

FILE 'SCISEARCH'
          5812 PHOSPHOENOLPYRUVATE
          80480 SYNTHASE#
L98          25 PHOSPHOENOLPYRUVATE SYNTHASE#
          (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)

FILE 'LIFESCI'
          2113 "PHOSPHOENOLPYRUVATE"
          19700 SYNTHASE#
L99          16 PHOSPHOENOLPYRUVATE SYNTHASE#
          ("PHOSPHOENOLPYRUVATE" (W) SYNTHASE#)

FILE 'BIOTECHDS'
          433 PHOSPHOENOLPYRUVATE
          4448 SYNTHASE#
L100         12 PHOSPHOENOLPYRUVATE SYNTHASE#
          (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)

FILE 'BIOSIS'
          7639 PHOSPHOENOLPYRUVATE
          78919 SYNTHASE#
L101         43 PHOSPHOENOLPYRUVATE SYNTHASE#
          (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)

FILE 'EMBASE'
          4238 "PHOSPHOENOLPYRUVATE"
          69481 SYNTHASE#
L102         23 PHOSPHOENOLPYRUVATE SYNTHASE#
          ("PHOSPHOENOLPYRUVATE" (W) SYNTHASE#)

FILE 'HCAPLUS'
          10663 PHOSPHOENOLPYRUVATE
          72314 SYNTHASE#
L103         107 PHOSPHOENOLPYRUVATE SYNTHASE#
          (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)

```

FILE 'NTIS'  
37 PHOSPHOENOLPYRUVATE  
202 SYNTHASE#  
L104 1 PHOSPHOENOLPYRUVATE SYNTHASE#  
(PHOSPHOENOLPYRUVATE (W) SYNTHASE#)

FILE 'ESBIOBASE'  
1799 PHOSPHOENOLPYRUVATE  
31769 SYNTHASE#  
L105 14 PHOSPHOENOLPYRUVATE SYNTHASE#  
(PHOSPHOENOLPYRUVATE (W) SYNTHASE#)

FILE 'BIOTECHNO'  
2400 PHOSPHOENOLPYRUVATE  
27132 SYNTHASE#  
L106 21 PHOSPHOENOLPYRUVATE SYNTHASE#  
(PHOSPHOENOLPYRUVATE (W) SYNTHASE#)

FILE 'WPIDS'  
200 PHOSPHOENOLPYRUVATE  
3209 SYNTHASE#  
L107 6 PHOSPHOENOLPYRUVATE SYNTHASE#  
(PHOSPHOENOLPYRUVATE (W) SYNTHASE#)

TOTAL FOR ALL FILES  
L108 295 PHOSPHOENOLPYRUVATE SYNTHASE#

=> s l108(5a)gene/q  
FILE 'MEDLINE'  
L109 3 L97 (5A) GENE/Q

FILE 'SCISEARCH'  
L110 5 L98 (5A) GENE/Q

FILE 'LIFESCI'  
L111 4 L99 (5A) GENE/Q

FILE 'BIOTECHDS'  
L112 4 L100 (5A) GENE/Q

FILE 'BIOSIS'  
L113 12 L101 (5A) GENE/Q

FILE 'EMBASE'  
L114 5 L102 (5A) GENE/Q

FILE 'HCAPLUS'  
L115 40 L103 (5A) GENE/Q

FILE 'NTIS'  
L116 0 L104 (5A) GENE/Q

FILE 'ESBIOBASE'  
L117 5 L105 (5A) GENE/Q

FILE 'BIOTECHNO'  
L118 5 L106 (5A) GENE/Q

FILE 'WPIDS'  
L119 2 L107 (5A) GENE/Q

TOTAL FOR ALL FILES  
L120 85 L108 (5A) GENE/Q

```

=> s (196 or 1120) and 124
FILE 'MEDLINE'
L121          2 (L85 OR L109) AND L13

FILE 'SCISEARCH'
L122          2 (L86 OR L110) AND L14

FILE 'LIFESCI'
L123          1 (L87 OR L111) AND L15

FILE 'BIOTECHDS'
L124          1 (L88 OR L112) AND L16

FILE 'BIOSIS'
L125          3 (L89 OR L113) AND L17

FILE 'EMBASE'
L126          2 (L90 OR L114) AND L18

FILE 'HCAPLUS'
L127          5 (L91 OR L115) AND L19

FILE 'NTIS'
L128          0 (L92 OR L116) AND L20

FILE 'ESBIOBASE'
L129          0 (L93 OR L117) AND L21

FILE 'BIOTECHNO'
L130          2 (L94 OR L118) AND L22

FILE 'WPIDS'
L131          2 (L95 OR L119) AND L23

TOTAL FOR ALL FILES
L132          20 (L96 OR L120) AND L24

=> s (196 or 1120) (5a) (overexpress? or amplif? or increas?)
FILE 'MEDLINE'
      46356 OVEREXPRESS?
      80503 AMPLIF?
      1739744 INCREAS?
L133          0 (L85 OR L109) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)

FILE 'SCISEARCH'
      53088 OVEREXPRESS?
      127002 AMPLIF?
      1690246 INCREAS?
L134          0 (L86 OR L110) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)

FILE 'LIFESCI'
      21016 OVEREXPRESS?
      40050 AMPLIF?
      448377 INCREAS?
L135          0 (L87 OR L111) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)

FILE 'BIOTECHDS'
      2961 OVEREXPRESS?
      23969 AMPLIF?
      54438 INCREAS?
L136          1 (L88 OR L112) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)

FILE 'BIOSIS'

```

51984 OVEREXPRESS?  
112383 AMPLIF?  
1890845 INCREAS?  
L137 2 (L89 OR L113) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)

FILE 'EMBASE'

43945 OVEREXPRESS?  
72465 AMPLIF?  
1642174 INCREAS?  
L138 0 (L90 OR L114) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)

FILE 'HCAPLUS'

47258 OVEREXPRESS?  
139970 AMPLIF?  
3493575 INCREAS?  
L139 32 (L91 OR L115) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)

FILE 'NTIS'

663 OVEREXPRESS?  
17648 AMPLIF?  
177108 INCREAS?  
L140 0 (L92 OR L116) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)

FILE 'ESBIOBASE'

33672 OVEREXPRESS?  
41555 AMPLIF?  
565029 INCREAS?  
L141 0 (L93 OR L117) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)

FILE 'BIOTECHNO'

32854 OVEREXPRESS?  
64034 AMPLIF?  
359617 INCREAS?  
L142 0 (L94 OR L118) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)

FILE 'WPIDS'

1692 OVEREXPRESS?  
228214 AMPLIF?  
1100016 INCREAS?  
L143 0 (L95 OR L119) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)

TOTAL FOR ALL FILES

L144 35 (L96 OR L120) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)

=> s (148 or 172 or 1132 or 1144) not 2001-2003/py

FILE 'MEDLINE'

1259962 2001-2003/PY  
L145 56 (L37 OR L61 OR L121 OR L133) NOT 2001-2003/PY

FILE 'SCISEARCH'

2305749 2001-2003/PY  
L146 89 (L38 OR L62 OR L122 OR L134) NOT 2001-2003/PY

FILE 'LIFESCI'

223576 2001-2003/PY  
L147 70 (L39 OR L63 OR L123 OR L135) NOT 2001-2003/PY

FILE 'BIOTECHDS'

46337 2001-2003/PY  
L148 4 (L40 OR L64 OR L124 OR L136) NOT 2001-2003/PY

FILE 'BIOSIS'

1215331 2001-2003/PY  
L149 134 (L41 OR L65 OR L125 OR L137) NOT 2001-2003/PY

FILE 'EMBASE'  
 1044608 2001-2003/PY  
 L150 67 (L42 OR L66 OR L126 OR L138) NOT 2001-2003/PY

FILE 'HCAPLUS'  
 2417906 2001-2003/PY  
 L151 154 (L43 OR L67 OR L127 OR L139) NOT 2001-2003/PY

FILE 'NTIS'  
 33435 2001-2003/PY  
 L152 0 (L44 OR L68 OR L128 OR L140) NOT 2001-2003/PY

FILE 'ESBIOBASE'  
 671253 2001-2003/PY  
 L153 54 (L45 OR L69 OR L129 OR L141) NOT 2001-2003/PY

FILE 'BIOTECHNO'  
 271276 2001-2003/PY  
 L154 57 (L46 OR L70 OR L130 OR L142) NOT 2001-2003/PY

FILE 'WPIDS'  
 2253073 2001-2003/PY  
 L155 2 (L47 OR L71 OR L131 OR L143) NOT 2001-2003/PY

TOTAL FOR ALL FILES  
 L156 687 (L48 OR L72 OR L132 OR L144) NOT 2001-2003/PY

=> save temp l156 pps/a  
 ANSWER SET L156 HAS BEEN SAVED AS 'PPS/A'

=> fil .becpat		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	15.27	15.48

FILES 'BIOTECHDS, HCAPLUS, WPIDS' ENTERED AT 13:35:32 ON 18 JUN 2003  
 ALL COPYRIGHTS AND RESTRICTIONS APPLY. SEE HELP USAGETERMS FOR DETAILS.

3 FILES IN THE FILE LIST

=> s (L48 OR L72 OR L132 OR L144) and wo/pc range=2001,  
 FILE 'BIOTECHDS'

1 GLNAP?  
 435 ACETYL  
 2853 PHOSPHATE  
 4 ACETYL PHOSPHATE  
 (ACETYL(W) PHOSPHATE)  
 1 ACETYLPHOSPHATE  
 1220 ACETATE  
 6659 PROMOTER?  
 7986 INDUC?  
 7160 REGULAT?  
 4931 ACTIVAT?  
 5560 MODULAT?  
 1513 L36(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)  
 435 ACETYL  
 2853 PHOSPHATE  
 4 ACETYL PHOSPHATE  
 (ACETYL(W) PHOSPHATE)  
 1 ACETYLPHOSPHATE  
 1220 ACETATE  
 6659 PROMOTER?  
 7986 INDUC?



7160 REGULAT?  
 4931 ACTIVAT?  
 5560 MODULAT?  
     4 L24 (8A) L36 (8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)  
     54 PHORBOL  
     12 TETRADECANOYLPORBOL  
 1220 ACETATE  
     21 (PHORBOL OR TETRADECANOYLPORBOL) (2A) ACETATE  
     47 PPS  
     70 PHOSPHOENOL  
     373 PYRUVATE  
 1221 SYNTHASE#  
     21 PHOSPHOENOL PYRUVATE SYNTHASE#  
         (PHOSPHOENOL (W) PYRUVATE (W) SYNTHASE#)  
     24 L84 (5A) GENE/Q  
     123 PHOSPHOENOLPYRUVATE  
 1221 SYNTHASE#  
     7 PHOSPHOENOLPYRUVATE SYNTHASE#  
         (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)  
     2 L108 (5A) GENE/Q  
     435 ACETYL  
 2853 PHOSPHATE  
     4 ACETYL PHOSPHATE  
         (ACETYL (W) PHOSPHATE)  
     1 ACETYLPHOSPHATE  
 1220 ACETATE  
     47 PPS  
     70 PHOSPHOENOL  
     373 PYRUVATE  
 1221 SYNTHASE#  
     21 PHOSPHOENOL PYRUVATE SYNTHASE#  
         (PHOSPHOENOL (W) PYRUVATE (W) SYNTHASE#)  
     123 PHOSPHOENOLPYRUVATE  
 1221 SYNTHASE#  
     7 PHOSPHOENOLPYRUVATE SYNTHASE#  
         (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)  
     2 L108 (5A) GENE/Q  
 1358 OVEREXPRESS?  
 12363 AMPLIF?  
 9844 INCREAS?  
     0 (L96 OR L120) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)  
 18816 WO/PC  
 L157      2 (L48 OR L72 OR L132 OR L144) AND WO/PC

FILE 'HCAPLUS'

    8 GLNAP?  
 10297 ACETYL  
 38524 PHOSPHATE  
     38 ACETYL PHOSPHATE  
         (ACETYL (W) PHOSPHATE)  
     11 ACETYLPHOSPHATE  
 37639 ACETATE  
 30651 PROMOTER?  
 241456 INDUC?  
 131943 REGULAT?  
 150909 ACTIVAT?  
 52604 MODULAT?  
     9951 L36 (8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)  
 10297 ACETYL  
 38524 PHOSPHATE  
     38 ACETYL PHOSPHATE  
         (ACETYL (W) PHOSPHATE)  
     11 ACETYLPHOSPHATE  
 37639 ACETATE

30651 PROMOTER?  
 241456 INDUC?  
 131943 REGULAT?  
 150909 ACTIVAT?  
 52604 MODULAT?  
     79 L24(8A) L36(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)  
     2927 PHORBOL  
     546 TETRADECANOYLPORBOL  
 37639 ACETATE  
     1321 (PHORBOL OR TETRADECANOYLPORBOL) (2A) ACETATE  
     567 PPS  
     134 PHOSPHOENOL  
     3064 PYRUVATE  
 17391 SYNTHASE#  
     4 PHOSPHOENOL PYRUVATE SYNTHASE#  
         (PHOSPHOENOL (W) PYRUVATE (W) SYNTHASE#)  
     48 L84(5A) GENE/Q  
     890 PHOSPHOENOLPYRUVATE  
 17391 SYNTHASE#  
     48 PHOSPHOENOLPYRUVATE SYNTHASE#  
         (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)  
     27 L108(5A) GENE/Q  
 10297 ACETYL  
 38524 PHOSPHATE  
     38 ACETYL PHOSPHATE  
         (ACETYL (W) PHOSPHATE)  
     11 ACETYLPHOSPHATE  
 37639 ACETATE  
     567 PPS  
     134 PHOSPHOENOL  
     3064 PYRUVATE  
 17391 SYNTHASE#  
     4 PHOSPHOENOL PYRUVATE SYNTHASE#  
         (PHOSPHOENOL (W) PYRUVATE (W) SYNTHASE#)  
     890 PHOSPHOENOLPYRUVATE  
 17391 SYNTHASE#  
     48 PHOSPHOENOLPYRUVATE SYNTHASE#  
         (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)  
     27 L108(5A) GENE/Q  
 16968 OVEREXPRESS?  
 32783 AMPLIF?  
 372311 INCREAS?  
     30 (L96 OR L120) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)  
 116278 WO/PC  
 L158      31 (L48 OR L72 OR L132 OR L144) AND WO/PC

FILE 'WPIDS'

    1 GLNAP?  
     2576 ACETYL  
 10353 PHOSPHATE  
     4 ACETYL PHOSPHATE  
         (ACETYL (W) PHOSPHATE)  
     1 ACETYLPHOSPHATE  
 11543 ACETATE  
     8533 PROMOTER?  
 35344 INDUC?  
 48515 REGULAT?  
 35722 ACTIVAT?  
 25328 MODULAT?  
     1721 L36(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)  
     2576 ACETYL  
 10353 PHOSPHATE  
     4 ACETYL PHOSPHATE  
         (ACETYL (W) PHOSPHATE)

```

1 ACETYLPHOSPHATE
11543 ACETATE
8533 PROMOTER?
35344 INDUC?
48515 REGULAT?
35722 ACTIVAT?
25328 MODULAT?
4 L24(8A) L36(8A) (INDUC? OR REGULAT? OR ACTIVAT? OR MODULAT?)
103 PHORBOL
14 TETRADECANOYLPHORBOL
11543 ACETATE
43 (PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE
210 PPS
82 PHOSPHOENOL
502 PYRUVATE
1457 SYNTHASE#
23 PHOSPHOENOL PYRUVATE SYNTHASE#
(PHOSPHOENOL(W) PYRUVATE(W) SYNTHASE#)
29 L84(5A) GENE/Q
120 PHOSPHOENOLPYRUVATE
1457 SYNTHASE#
4 PHOSPHOENOLPYRUVATE SYNTHASE#
(PHOSPHOENOLPYRUVATE(W) SYNTHASE#)
1 L108(5A) GENE/Q
2576 ACETYL
10353 PHOSPHATE
4 ACETYL PHOSPHATE
(ACETYL(W) PHOSPHATE)
1 ACETYLPHOSPHATE
11543 ACETATE
210 PPS
82 PHOSPHOENOL
502 PYRUVATE
1457 SYNTHASE#
23 PHOSPHOENOL PYRUVATE SYNTHASE#
(PHOSPHOENOL(W) PYRUVATE(W) SYNTHASE#)
120 PHOSPHOENOLPYRUVATE
1457 SYNTHASE#
4 PHOSPHOENOLPYRUVATE SYNTHASE#
(PHOSPHOENOLPYRUVATE(W) SYNTHASE#)
1 L108(5A) GENE/Q
1006 OVEREXPRESS?
29761 AMPLIF?
151517 INCREAS?
0 (L96 OR L120) (5A) (OVEREXPRESS? OR AMPLIF? OR INCREAS?)
248323 WO/PC
L159 2 (L48 OR L72 OR L132 OR L144) AND WO/PC

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TOTAL FOR ALL FILES

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L160 35 (L48 OR L72 OR L132 OR L144) AND WO/PC

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=> dup rem l160

PROCESSING COMPLETED FOR L160

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L161 32 DUP REM L160 (3 DUPLICATES REMOVED)

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=> d tot

```

L161 ANSWER 1 OF 32 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
TI Method for the production of pyruvate in high conversion and yield,
comprises carrying out fermentation using microorganisms with reduced or
eliminated activity of pyruvate decomposing enzymes;
pyruvic acid preparation by mutant bacterium fermentation
AU BOTT M; GERHARZ T; TAKORS R; ZELIC B
AN 2003-10747 BIOTECHDS

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PI WO 20030000913 3 Jan 2003

L161 ANSWER 2 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing genes iclR and fadR for fermentative prodn. of threonine

SO PCT Int. Appl., 34 pp.

CODEN: PIXXD2

IN Rieping, Mechthild; Siebelt, Nicole

AN 2003:356618 HCAPLUS

DN 138:363837

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003038106	A2	20030508	WO 2002-EP10791	20020926 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10154102	A1	20030515	DE 2001-10154102	20011102

L161 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli for the fermentative production of threonine containing an attenuated aceK gene

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

IN Hermann, Thomas

AN 2003:76954 HCAPLUS

DN 138:132163

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008616	A2	20030130	WO 2002-EP7353	20020703 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10135051	A1	20030206	DE 2001-10135051	20010718

L161 ANSWER 4 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing genes sucC and sucD for the fermentative production of threonine

SO PCT Int. Appl., 30 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:76953 HCAPLUS

DN 138:132162

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008615	A2	20030130	WO 2002-EP7375	20020703 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
 TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
 NE, SN, TD, TG

DE 10135053 A1 20030206 DE 2001-10135053 20010718

L161 ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing genes sucA and sucB  
 for the fermentative production of threonine

SO PCT Int. Appl., 28 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:76952 HCAPLUS

DN 138:132161

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003008614	A2	20030130	WO 2002-EP7374	20020703 <--
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
 TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
 NE, SN, TD, TG

DE 10135053 A1 20030206 DE 2001-10135053 20010718

L161 ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing gene sodA for the  
 fermentative production of threonine

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:76951 HCAPLUS

DN 138:132160

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003008613	A2	20030130	WO 2002-EP7373	20020703 <--
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
 TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
 NE, SN, TD, TG

DE 10135053 A1 20030206 DE 2001-10135053 20010718

L161 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing genes rseA or rseC  
 for the fermentative production of threonine

SO PCT Int. Appl., 33 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:76950 HCAPLUS  
DN 138:132159

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003008612	A2	20030130	WO 2002-EP7370	20020703 <--
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	DE 10135053	A1	20030206	DE 2001-10135053	20010718

L161 ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing gene talB for the fermentative production of threonine

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:76949 HCAPLUS

DN 138:132158

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003008611	A2	20030130	WO 2002-EP7369	20020703 <--
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	DE 10135053	A1	20030206	DE 2001-10135053	20010718

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TI Genetically modified Escherichia coli overexpressing gene pfkB for the fermentative production of threonine

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:76948 HCAPLUS

DN 138:132157

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003008610	A2	20030130	WO 2002-EP7368	20020703 <--
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

DE 10135053      A1      20030206      DE 2001-10135053 20010718

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TI Genetically modified Escherichia coli overexpressing gene pykF for the fermentative production of threonine

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:76947 HCAPLUS

DN 138:132156

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003008609	A2	20030130	WO 2002-EP7367	20020703	<--
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10135053      A1      20030206      DE 2001-10135053 20010718

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TI Genetically modified Escherichia coli overexpressing gene phoE for the fermentative production of threonine

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:76946 HCAPLUS

DN 138:132155

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003008608	A2	20030130	WO 2002-EP7366	20020703	<--
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10135053      A1      20030206      DE 2001-10135053 20010718

L161 ANSWER 12 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli for the fermentative production of threonine

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:76945 HCAPLUS

DN 138:118453

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003008607	A2	20030130	WO 2002-EP7356	20020703	<--
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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
 TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
 NE, SN, TD, TG

DE 10135053 A1 20030206 DE 2001-10135053 20010718

L161 ANSWER 13 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing genes phoB and phoR  
 for the fermentative production of threonine

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:76944 HCAPLUS

DN 138:132154

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008606	A2	20030130	WO 2002-EP7355	20020703 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
 TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
 NE, SN, TD, TG

DE 10135053 A1 20030206 DE 2001-10135053 20010718

L161 ANSWER 14 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing gene male for the  
 fermentative production of threonine

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:76943 HCAPLUS

DN 138:132153

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008605	A2	20030130	WO 2002-EP7354	20020703 <--

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 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
 TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
 NE, SN, TD, TG

DE 10135053 A1 20030206 DE 2001-10135053 20010718

L161 ANSWER 15 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli for the fermentative production of  
 threonine containing an attenuated aceB gene

SO PCT Int. Appl., 36 pp.

CODEN: PIXXD2

IN Hermann, Thomas



AN 2003:76942 HCAPLUS  
DN 138:132152

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003008604	A2	20030130	WO 2002-EP7352	20020703 <--
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	DE 10135051	A1	20030206	DE 2001-10135051	20010718

L161 ANSWER 16 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli for the fermentative production of threonine containing an attenuated aspA gene

SO PCT Int. Appl., 36 pp.

CODEN: PIXXD2

IN Hermann, Thomas

AN 2003:76941 HCAPLUS

DN 138:132151

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003008603	A2	20030130	WO 2002-EP7351	20020703 <--
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	DE 10135051	A1	20030206	DE 2001-10135051	20010718

L161 ANSWER 17 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli for the fermentative production of threonine containing an attenuated ugpB gene

SO PCT Int. Appl., 35 pp.

CODEN: PIXXD2

IN Hermann, Thomas

AN 2003:76940 HCAPLUS

DN 138:132150

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003008602	A2	20030130	WO 2002-EP7350	20020703 <--
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

DE 10135051

A1 20030206

DE 2001-10135051 20010718

L161 ANSWER 18 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing genes of the cysteine biosynthesis pathway for the fermentative production of threonine

SO PCT Int. Appl., 58 pp.

CODEN: PIXXD2

IN Siebelt, Nicole; Widawka, Petra; Farwick, Mike

AN 2003:58256 HCAPLUS

DN 138:118448

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003006666	A2	20030123	WO 2002-EP6187	20020606 <--
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10133667

A1 20030130

DE 2001-10133667 20010711

L161 ANSWER 19 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing gene dps for the fermentative production of threonine

SO PCT Int. Appl., 26 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:42431 HCAPLUS

DN 138:84490

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003004675	A2	20030116	WO 2002-EP6568	20020614 <--
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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DE 10132946

A1 20030116

DE 2001-10132946 20010706

L161 ANSWER 20 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing genes crr, ptsH, and ptsI for the fermentative production of threonine

SO PCT Int. Appl., 26 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:42430 HCAPLUS

DN 138:84489

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003004674	A2	20030116	WO 2002-EP6562	20020614 <--
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 DE 10132946 A1 20030116 DE 2001-10132946 20010706

L161 ANSWER 21 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing gene hns for the fermentative production of threonine

SO PCT Int. Appl., 25 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:42427 HCAPLUS

DN 138:101972

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004671	A2	20030116	WO 2002-EP6567	20020614 <--
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DE 10132946	A1	20030116	DE 2001-10132946	20010706

L161 ANSWER 22 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing gene ptsG for the fermentative production of threonine

SO PCT Int. Appl., 25 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:42426 HCAPLUS

DN 138:84488

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004670	A2	20030116	WO 2002-EP6563	20020614 <--
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DE 10132946	A1	20030116	DE 2001-10132946	20010706

L161 ANSWER 23 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing gene mopB for the fermentative production of threonine

SO PCT Int. Appl., 25 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:42425 HCAPLUS

DN 138:84487

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004669	A2	20030116	WO 2002-EP6561	20020614 <--

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DE 10132946 A1 20030116 DE 2001-10132946 20010706

L161 ANSWER 24 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing gene lrp for the fermentative production of threonine

SO PCT Int. Appl., 25 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:42422 HCAPLUS

DN 138:84486

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004665	A2	20030116	WO 2002-EP6566	20020614 <--
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DE 10132946	A1	20030116	DE 2001-10132946	20010706

L161 ANSWER 25 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing gene fba for the fermentative production of threonine

SO PCT Int. Appl., 25 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:42421 HCAPLUS

DN 138:84485

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004664	A2	20030116	WO 2002-EP6564	20020614 <--
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DE 10132946	A1	20030116	DE 2001-10132946	20010706

L161 ANSWER 26 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing genes ahpC and ahpF for the fermentative production of threonine

SO PCT Int. Appl., 25 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:42420 HCAPLUS  
DN 138:84484

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003004663	A2	20030116	WO 2002-EP6560	20020614 <--
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	DE 10132946	A1	20030116	DE 2001-10132946	20010706

L161 ANSWER 27 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli strains for the fermentative production of threonine

SO PCT Int. Appl., 21 pp.

CODEN: PIXXD2

IN Hermann, Thomas

AN 2003:42419 HCAPLUS

DN 138:84483

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003004662	A2	20030116	WO 2002-EP5169	20020510 <--
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	DE 10132945	A1	20030116	DE 2001-10132945	20010706
	US 2003017556	A1	20030123	US 2002-186999	20020703

L161 ANSWER 28 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Genetically modified Escherichia coli overexpressing gene pgm for the fermentative production of threonine

SO PCT Int. Appl., 25 pp.

CODEN: PIXXD2

IN Rieping, Mechthild

AN 2003:42360 HCAPLUS

DN 138:84481

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2003004598	A2	20030116	WO 2002-EP6565	20020614 <--
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	DE 10132946	A1	20030116	DE 2001-10132946	20010706

L161 ANSWER 29 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Sequences of ppsA gene from corynebacteria and use thereof in production of L-lysine  
 SO PCT Int. Appl., 29 pp.  
 CODEN: PIXXD2  
 IN Moeckel, Bettina; Marx, Achim; Bastuck, Christine; Buchholz, Michael; Pfefferle, Walter  
 AN 2002:220797 HCAPLUS  
 DN 136:261908

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2002022829	A2	20020321	WO 2001-EP9456	20010816 <--
WO 2002022829	A3	20020711		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10045497	A1	20020328	DE 2000-10045497	20000913
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AU 2002014949	A5	20020326	AU 2002-14949	20010816
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EP 1317550	A2	20030611	EP 2001-983438	20010816
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US 2002045224	A1	20020418	US 2001-946141	20010905
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L161 ANSWER 30 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Recombinant Enterobacteriaceae overexpressing malate:quinone oxidoreductase gene mqo and their use in threonine production  
 SO PCT Int. Appl., 39 pp.  
 CODEN: PIXXD2

IN Rieping, Mechthild; Thierbach, Georg; Van Der Rest, Michel Eduard; Molenaar, Douwe  
 AN 2002:72263 HCAPLUS  
 DN 136:133691

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2002006459	A1	20020124	WO 2001-EP5548	20010516 <--
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DE 10103874	A1	20020131	DE 2001-10103874	20010130
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US 2002127678	A1	20020912	US 2001-801042	20010308
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EP 1303590	A1	20030423	EP 2001-943376	20010516
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L161 ANSWER 31 OF 32 HCAPLUS COPYRIGHT 2003 ACS

TI Fermentative production of L-amino acids with poxB mutants of Enterobacteriaceae  
 SO Ger. Offen., 22 pp.  
 CODEN: GWXXBX

IN Thierbach, Georg; Rieping, Mechthild  
 AN 2002:349112 HCAPLUS  
 DN 136:354249

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI  DE 10112107      A1  20020508      DE 2001-10112107 20010314
    WO 2002036797    A2  20020510      WO 2001-EP11228 20010928 <--
    WO 2002036797    A3  20021114
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        BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    AU 2002015910      A5  20020515      AU 2002-15910      20010928
    US 2003017554      A1  20030123      US 2002-76416      20020219

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L161 ANSWER 32 OF 32 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI  
 TI Engineering metabolic control, e.g. using promoters in specific host  
 cells to optimize protein expression for either protein production or  
 metabolite synthesis;

lycopene and isoprenoid production by metabolic engineering of  
 Escherichia coli

AU Liao J C  
 AN 2001-06913 BIOTECHDS  
 PI WO 2001007567 1 Feb 2001

=> fil .bec

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
58.38	73.86

FULL ESTIMATED COST

FILES 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS,  
 ESBIODBASE, BIOTECHNO, WPIDS' ENTERED AT 13:41:40 ON 18 JUN 2003  
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11 FILES IN THE FILE LIST

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9357 ISOPREN?  
 1131 LYCOPENE#  
 12510 CAROTEN?

L162 21806 ISOPREN? OR LYCOPENE# OR CAROTEN?

FILE 'SCISEARCH'

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 18276 CAROTEN?

L163 29214 ISOPREN? OR LYCOPENE# OR CAROTEN?

FILE 'LIFESCI'

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FILE 'NTIS'

321 ISOPREN?  
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285 CAROTEN?  
L169 608 ISOPREN? OR LYCOPENE# OR CAROTEN?

FILE 'ESBIOBASE'

2945 ISOPREN?  
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5252 CAROTEN?  
L170 8207 ISOPREN? OR LYCOPENE# OR CAROTEN?

FILE 'BIOTECHNO'

4472 ISOPREN?  
278 LYCOPENE#  
2569 CAROTEN?  
L171 7003 ISOPREN? OR LYCOPENE# OR CAROTEN?

FILE 'WPIDS'

13493 ISOPREN?  
331 LYCOPENE#  
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L172 16610 ISOPREN? OR LYCOPENE# OR CAROTEN?

TOTAL FOR ALL FILES

L173 276009 ISOPREN? OR LYCOPENE# OR CAROTEN?

=> s l173 and l108

FILE 'MEDLINE'

6309 PHOSPHOENOLPYRUVATE  
71061 SYNTHASE#  
27 PHOSPHOENOLPYRUVATE SYNTHASE#  
(PHOSPHOENOLPYRUVATE(W) SYNTHASE#)  
L174 0 L162 AND L108

FILE 'SCISEARCH'

5812 PHOSPHOENOLPYRUVATE  
80480 SYNTHASE#  
25 PHOSPHOENOLPYRUVATE SYNTHASE#  
(PHOSPHOENOLPYRUVATE(W) SYNTHASE#)  
L175 0 L163 AND L108

FILE 'LIFESCI'

2113 "PHOSPHOENOLPYRUVATE"  
19700 SYNTHASE#  
16 PHOSPHOENOLPYRUVATE SYNTHASE#  
( "PHOSPHOENOLPYRUVATE" (W) SYNTHASE#)



L176            0 L164 AND L108  
  
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 L177            0 L165 AND L108  
  
 FILE 'BIOSIS'  
     7639 PHOSPHOENOLPYRUVATE  
    78919 SYNTHASE#  
       43 PHOSPHOENOLPYRUVATE SYNTHASE#  
         (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)  
 L178            0 L166 AND L108  
  
 FILE 'EMBASE'  
     4238 "PHOSPHOENOLPYRUVATE"  
    69481 SYNTHASE#  
       23 PHOSPHOENOLPYRUVATE SYNTHASE#  
         ("PHOSPHOENOLPYRUVATE" (W) SYNTHASE#)  
 L179            0 L167 AND L108  
  
 FILE 'HCAPLUS'  
    10665 PHOSPHOENOLPYRUVATE  
    72350 SYNTHASE#  
       107 PHOSPHOENOLPYRUVATE SYNTHASE#  
         (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)  
 L180            3 L168 AND L108  
  
 FILE 'NTIS'  
     37 PHOSPHOENOLPYRUVATE  
    202 SYNTHASE#  
       1 PHOSPHOENOLPYRUVATE SYNTHASE#  
         (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)  
 L181            0 L169 AND L108  
  
 FILE 'ESBIOBASE'  
    1799 PHOSPHOENOLPYRUVATE  
   31769 SYNTHASE#  
       14 PHOSPHOENOLPYRUVATE SYNTHASE#  
         (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)  
 L182            0 L170 AND L108  
  
 FILE 'BIOTECHNO'  
    2400 PHOSPHOENOLPYRUVATE  
   27132 SYNTHASE#  
       21 PHOSPHOENOLPYRUVATE SYNTHASE#  
         (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)  
 L183            0 L171 AND L108  
  
 FILE 'WPIDS'  
    200 PHOSPHOENOLPYRUVATE  
   3209 SYNTHASE#  
       6 PHOSPHOENOLPYRUVATE SYNTHASE#  
         (PHOSPHOENOLPYRUVATE (W) SYNTHASE#)  
 L184            1 L172 AND L108  
  
 TOTAL FOR ALL FILES  
 L185            4 L173 AND L108  
  
 => s l173 and l84  
 FILE 'MEDLINE'  
    2102 PPS

226 PHOSPHOENOL  
 23418 PYRUVATE  
 71061 SYNTHASE#  
 0 PHOSPHOENOL PYRUVATE SYNTHASE#  
 (PHOSPHOENOL (W) PYRUVATE (W) SYNTHASE#)  
 L186 2 L162 AND L84

FILE 'SCISEARCH'  
 1957 PPS  
 220 PHOSPHOENOL  
 18316 PYRUVATE  
 80480 SYNTHASE#  
 1 PHOSPHOENOL PYRUVATE SYNTHASE#  
 (PHOSPHOENOL (W) PYRUVATE (W) SYNTHASE#)  
 L187 4 L163 AND L84

FILE 'LIFESCI'  
 328 PPS  
 114 "PHOSPHOENOL"  
 5779 "PYRUVATE"  
 19700 SYNTHASE#  
 0 PHOSPHOENOL PYRUVATE SYNTHASE#  
 ("PHOSPHOENOL" (W) "PYRUVATE" (W) SYNTHASE#)  
 L188 1 L164 AND L84

FILE 'BIOTECHDS'  
 107 PPS  
 104 PHOSPHOENOL  
 1784 PYRUVATE  
 4448 SYNTHASE#  
 21 PHOSPHOENOL PYRUVATE SYNTHASE#  
 (PHOSPHOENOL (W) PYRUVATE (W) SYNTHASE#)  
 L189 0 L165 AND L84

FILE 'BIOSIS'  
 1096 PPS  
 3651 PHOSPHOENOL  
 34782 PYRUVATE  
 78919 SYNTHASE#  
 11 PHOSPHOENOL PYRUVATE SYNTHASE#  
 (PHOSPHOENOL (W) PYRUVATE (W) SYNTHASE#)  
 L190 3 L166 AND L84

FILE 'EMBASE'  
 1381 PPS  
 173 "PHOSPHOENOL"  
 19215 "PYRUVATE"  
 69481 SYNTHASE#  
 0 PHOSPHOENOL PYRUVATE SYNTHASE#  
 ("PHOSPHOENOL" (W) "PYRUVATE" (W) SYNTHASE#)  
 L191 5 L167 AND L84

FILE 'HCAPLUS'  
 2657 PPS  
 676 PHOSPHOENOL  
 46733 PYRUVATE  
 72350 SYNTHASE#  
 7 PHOSPHOENOL PYRUVATE SYNTHASE#  
 (PHOSPHOENOL (W) PYRUVATE (W) SYNTHASE#)  
 L192 7 L168 AND L84

FILE 'NTIS'  
 689 PPS  
 5 PHOSPHOENOL

```

304 PYRUVATE
202 SYNTHASE#
  0 PHOSPHOENOL PYRUVATE SYNTHASE#
    (PHOSPHOENOL(W) PYRUVATE(W) SYNTHASE#)
L193      0 L169 AND L84

FILE 'ESBIOBASE'
  419 PPS
  72 PHOSPHOENOL
  5427 PYRUVATE
  31769 SYNTHASE#
    0 PHOSPHOENOL PYRUVATE SYNTHASE#
      (PHOSPHOENOL(W) PYRUVATE(W) SYNTHASE#)
L194      0 L170 AND L84

FILE 'BIOTECHNO'
  231 PPS
  77 PHOSPHOENOL
  6261 PYRUVATE
  27132 SYNTHASE#
    0 PHOSPHOENOL PYRUVATE SYNTHASE#
      (PHOSPHOENOL(W) PYRUVATE(W) SYNTHASE#)
L195      1 L171 AND L84

FILE 'WPIDS'
  1273 PPS
  166 PHOSPHOENOL
  1620 PYRUVATE
  3209 SYNTHASE#
  24 PHOSPHOENOL PYRUVATE SYNTHASE#
    (PHOSPHOENOL(W) PYRUVATE(W) SYNTHASE#)
L196      1 L172 AND L84

TOTAL FOR ALL FILES
L197      24 L173 AND L84

=> s l173 and (l24 not ((PHORBOL OR TETRADECANOYLPORBOL) (2A) ACETATE))
FILE 'MEDLINE'
  37029 ACETYL
  123607 PHOSPHATE
  324 ACETYL PHOSPHATE
    (ACETYL(W) PHOSPHATE)
  71 ACETYLPHOSPHATE
  86014 ACETATE
  31039 PHORBOL
  26731 TETRADECANOYLPORBOL
  86014 ACETATE
  30444 (PHORBOL OR TETRADECANOYLPORBOL) (2A) ACETATE
L198      355 L162 AND (L24 NOT ((PHORBOL OR TETRADECANOYLPORBOL) (2A) ACETATE
    ))

FILE 'SCISEARCH'
  36635 ACETYL
  127161 PHOSPHATE
  311 ACETYL PHOSPHATE
    (ACETYL(W) PHOSPHATE)
  34 ACETYLPHOSPHATE
  83662 ACETATE
  29522 PHORBOL
  4491 TETRADECANOYLPORBOL
  83662 ACETATE
  11169 (PHORBOL OR TETRADECANOYLPORBOL) (2A) ACETATE
L199      563 L163 AND (L24 NOT ((PHORBOL OR TETRADECANOYLPORBOL) (2A) ACETATE
    ))

```

FILE 'LIFESCI'

10624 "ACETYL"  
 36365 "PHOSPHATE"  
 166 ACETYL PHOSPHATE  
 ("ACETYL" (W) "PHOSPHATE")  
 22 ACETYLPHOSPHATE  
 23165 ACETATE  
 11370 PHORBOL  
 2294 TETRADECANOYLPHORPOL  
 23165 ACETATE  
 5584 (PHORBOL OR TETRADECANOYLPHORPOL) (2A) ACETATE  
 L200 118 L164 AND (L24 NOT ((PHORBOL OR TETRADECANOYLPHORPOL) (2A) ACETATE  
 ))

FILE 'BIOTECHDS'

2604 ACETYL  
 15692 PHOSPHATE  
 48 ACETYL PHOSPHATE  
 (ACETYL (W) PHOSPHATE)  
 11 ACETYLPHOSPHATE  
 11055 ACETATE  
 274 PHORBOL  
 47 TETRADECANOYLPHORPOL  
 11055 ACETATE  
 149 (PHORBOL OR TETRADECANOYLPHORPOL) (2A) ACETATE  
 L201 77 L165 AND (L24 NOT ((PHORBOL OR TETRADECANOYLPHORPOL) (2A) ACETATE  
 ))

FILE 'BIOSIS'

83598 ACETYL  
 186290 PHOSPHATE  
 422 ACETYL PHOSPHATE  
 (ACETYL (W) PHOSPHATE)  
 78 ACETYLPHOSPHATE  
 112682 ACETATE  
 37478 PHORBOL  
 9328 TETRADECANOYLPHORPOL  
 112682 ACETATE  
 21297 (PHORBOL OR TETRADECANOYLPHORPOL) (2A) ACETATE  
 L202 677 L166 AND (L24 NOT ((PHORBOL OR TETRADECANOYLPHORPOL) (2A) ACETATE  
 ))

FILE 'EMBASE'

38373 "ACETYL"  
 151764 "PHOSPHATE"  
 265 ACETYL PHOSPHATE  
 ("ACETYL" (W) "PHOSPHATE")  
 40 ACETYLPHOSPHATE  
 99814 ACETATE  
 36797 PHORBOL  
 5982 TETRADECANOYLPHORPOL  
 99814 ACETATE  
 24891 (PHORBOL OR TETRADECANOYLPHORPOL) (2A) ACETATE  
 L203 766 L167 AND (L24 NOT ((PHORBOL OR TETRADECANOYLPHORPOL) (2A) ACETATE  
 ))

FILE 'HCAPLUS'

133044 ACETYL  
 482932 PHOSPHATE  
 925 ACETYL PHOSPHATE  
 (ACETYL (W) PHOSPHATE)  
 236 ACETYLPHOSPHATE  
 449484 ACETATE

30933 PHORBOL  
6319 TETRADECANOYLPHORBOL  
449484 ACETATE  
15768 (PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE  
L204 4128 L168 AND (L24 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE  
))

FILE 'NTIS'

725 ACETYL  
6281 PHOSPHATE  
1 ACETYL PHOSPHATE  
(ACETYL(W) PHOSPHATE)  
1 ACETYLPHOSPHATE  
3039 ACETATE  
194 PHORBOL  
29 TETRADECANOYLPHORBOL  
3039 ACETATE  
80 (PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE  
L205 7 L169 AND (L24 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE  
))

FILE 'ESBIOBASE'

11210 ACETYL  
35348 PHOSPHATE  
135 ACETYL PHOSPHATE  
(ACETYL(W) PHOSPHATE)  
16 ACETYLPHOSPHATE  
22040 ACETATE  
10955 PHORBOL  
1968 TETRADECANOYLPHORBOL  
22040 ACETATE  
4576 (PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE  
L206 191 L170 AND (L24 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE  
))

FILE 'BIOTECHNO'

11762 ACETYL  
48786 PHOSPHATE  
184 ACETYL PHOSPHATE  
(ACETYL(W) PHOSPHATE)  
28 ACETYLPHOSPHATE  
28164 ACETATE  
18056 PHORBOL  
3163 TETRADECANOYLPHORBOL  
28164 ACETATE  
11969 (PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE  
L207 161 L171 AND (L24 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE  
))

FILE 'WPIDS'

23959 ACETYL  
79708 PHOSPHATE  
31 ACETYL PHOSPHATE  
(ACETYL(W) PHOSPHATE)  
17 ACETYLPHOSPHATE  
109139 ACETATE  
288 PHORBOL  
40 TETRADECANOYLPHORBOL  
109139 ACETATE  
137 (PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE  
L208 1569 L172 AND (L24 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE  
))

TOTAL FOR ALL FILES

L209        8612 L173 AND (L24 NOT ((PHORBOL OR TETRADECANOYLPHORBOL) (2A) ACETATE  
              ))

=> s l173(5a) (synthes? or production# or mak?)

FILE 'MEDLINE'

      427413 SYNTHES?

      305768 PRODUCTION#

      247920 MAK?

L210        846 L162(5A) (SYNTHES? OR PRODUCTION# OR MAK?)

FILE 'SCISEARCH'

      739600 SYNTHES?

      479606 PRODUCTION#

      266667 MAK?

L211        1635 L163(5A) (SYNTHES? OR PRODUCTION# OR MAK?)

FILE 'LIFESCI'

      126867 SYNTHES?

      161711 PRODUCTION#

      45002 MAK?

L212        533 L164(5A) (SYNTHES? OR PRODUCTION# OR MAK?)

FILE 'BIOTECHDS'

      25939 SYNTHES?

      107549 PRODUCTION#

      8620 MAK?

L213        404 L165(5A) (SYNTHES? OR PRODUCTION# OR MAK?)

FILE 'BIOSIS'

      584576 SYNTHES?

      543711 PRODUCTION#

      163135 MAK?

L214        2178 L166(5A) (SYNTHES? OR PRODUCTION# OR MAK?)

FILE 'EMBASE'

      523551 SYNTHES?

      316131 PRODUCTION#

      213006 MAK?

L215        772 L167(5A) (SYNTHES? OR PRODUCTION# OR MAK?)

FILE 'HCAPLUS'

      1296882 SYNTHES?

      493972 PRODUCTION#

      759068 PRODN

      1053236 PRODUCTION#

              (PRODUCTION# OR PRODN)

      495793 MAK?

L216        4967 L168(5A) (SYNTHES? OR PRODUCTION# OR MAK?)

FILE 'NTIS'

      41089 SYNTHES?

      129891 PRODUCTION#

      114971 MAK?

L217        21 L169(5A) (SYNTHES? OR PRODUCTION# OR MAK?)

FILE 'ESBIOBASE'

      148053 SYNTHES?

      150320 PRODUCTION#

      50602 MAK?

L218        562 L170(5A) (SYNTHES? OR PRODUCTION# OR MAK?)

FILE 'BIOTECHNO'

      162184 SYNTHES?

      140843 PRODUCTION#

32178 MAK?  
 L219 468 L171(5A) (SYNTHES? OR PRODUCTION# OR MAK?)  
 FILE 'WPIDS'  
 106127 SYNTHES?  
 298074 PRODUCTION#  
 473786 PRODN  
 753376 PRODUCTION#  
 (PRODUCTION# OR PRODN)  
 558784 MAK?  
 L220 1019 L172(5A) (SYNTHES? OR PRODUCTION# OR MAK?)  
 TOTAL FOR ALL FILES  
 L221 13405 L173(5A) (SYNTHES? OR PRODUCTION# OR MAK?)  
 => s l209 and l221  
 FILE 'MEDLINE'  
 L222 35 L198 AND L210  
 FILE 'SCISEARCH'  
 L223 42 L199 AND L211  
 FILE 'LIFESCI'  
 L224 17 L200 AND L212  
 FILE 'BIOTECHDS'  
 L225 9 L201 AND L213  
 FILE 'BIOSIS'  
 L226 72 L202 AND L214  
 FILE 'EMBASE'  
 L227 32 L203 AND L215  
 FILE 'HCAPLUS'  
 L228 280 L204 AND L216  
 FILE 'NTIS'  
 L229 2 L205 AND L217  
 FILE 'ESBIOBASE'  
 L230 22 L206 AND L218  
 FILE 'BIOTECHNO'  
 L231 15 L207 AND L219  
 FILE 'WPIDS'  
 L232 45 L208 AND L220  
 TOTAL FOR ALL FILES  
 L233 571 L209 AND L221  
 => s (l185 or l197 or l233) not 2001-2003/py  
 FILE 'MEDLINE'  
 1261926 2001-2003/PY  
 L234 35 (L174 OR L186 OR L222) NOT 2001-2003/PY  
 FILE 'SCISEARCH'  
 2305749 2001-2003/PY  
 L235 43 (L175 OR L187 OR L223) NOT 2001-2003/PY  
 FILE 'LIFESCI'  
 223576 2001-2003/PY  
 L236 17 (L176 OR L188 OR L224) NOT 2001-2003/PY

FILE 'BIOTECHDS'  
46337 2001-2003/PY  
L237 5 (L177 OR L189 OR L225) NOT 2001-2003/PY

FILE 'BIOSIS'  
1215331 2001-2003/PY  
L238 70 (L178 OR L190 OR L226) NOT 2001-2003/PY

FILE 'EMBASE'  
1044608 2001-2003/PY  
L239 34 (L179 OR L191 OR L227) NOT 2001-2003/PY

FILE 'HCAPLUS'  
2421784 2001-2003/PY  
L240 255 (L180 OR L192 OR L228) NOT 2001-2003/PY

FILE 'NTIS'  
33435 2001-2003/PY  
L241 1 (L181 OR L193 OR L229) NOT 2001-2003/PY

FILE 'ESBIOBASE'  
671253 2001-2003/PY  
L242 19 (L182 OR L194 OR L230) NOT 2001-2003/PY

FILE 'BIOTECHNO'  
271276 2001-2003/PY  
L243 14 (L183 OR L195 OR L231) NOT 2001-2003/PY

FILE 'WPIDS'  
2253073 2001-2003/PY  
L244 28 (L184 OR L196 OR L232) NOT 2001-2003/PY

TOTAL FOR ALL FILES  
L245 521 (L185 OR L197 OR L233) NOT 2001-2003/PY

=> dup rem l245  
PROCESSING COMPLETED FOR L245  
L246 324 DUP REM L245 (197 DUPLICATES REMOVED)

=> d tot

L246 ANSWER 1 OF 324 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI  
TI Manufacture of actinol useful for **synthesizing**  
**carotenoids** by selective asymmetric reduction of levodione with  
new Cellulomonas, Corynebacterium, Planococcus and Arthrobacter  
microorganisms;  
production of actinol by reacting Cellulomonas species,  
Corynebacterium aquaticum, Planococcus akeanokoites or Arthrobacter  
sulfureus with levodione  
AU Shimizu S; Wada M  
AN 2000-06238 BIOTECHDS  
PI EP 982406 1 Mar 2000

L246 ANSWER 2 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI The use of cholesterol-synthesis inhibitors for the reduction of the level  
of cholesterol in poultry eggs  
SO Eur. Pat. Appl., 19 pp.  
CODEN: EPXXDW  
IN Kramer, Klaus; Baldenius, Kai-Uwe; Hoppe, Peter Paul  
AN 2000:98040 HCAPLUS  
DN 132:136828

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 978236	A1	20000209	EP 1999-115698	19990809
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	DE 19835850	A1	20000210	DE 1998-19835850	19980807
	US 6166067	A	20001226	US 1999-362062	19990728
	JP 2000060435	A2	20000229	JP 1999-221602	19990804
	CN 1258457	A	20000705	CN 1999-119696	19990807

L246 ANSWER 3 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 1  
 TI Effect of the solvent environment on the spectroscopic properties and  
 dynamics of the lowest excited states of **carotenoids**  
 SO JOURNAL OF PHYSICAL CHEMISTRY B, (11 MAY 2000) Vol. 104, No. 18, pp.  
 4569-4577.  
 Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.  
 ISSN: 1089-5647.  
 AU Frank H A (Reprint); Bautista J A; Josue J; Pendon Z; Hiller R G; Sharples  
 F P; Gosztola D; Wasielewski M R  
 AN 2000:376281 SCISEARCH

L246 ANSWER 4 OF 324 MEDLINE DUPLICATE 2  
 TI Antioxidant activity of dietary polyphenols as determined by a modified  
 ferric reducing/antioxidant power assay.  
 SO JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY, (2000 Aug) 48 (8) 3396-402.  
 Journal code: 0374755. ISSN: 0021-8561.  
 AU Pulido R; Bravo L; Saura-Calixto F  
 AN 2000458862 MEDLINE

L246 ANSWER 5 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Design and Synthesis of a Transferable Farnesyl Pyrophosphate Analogue to  
 Ras by Protein Farnesyltransferase  
 SO Journal of Organic Chemistry (2000), 65(10), 3027-3033  
 CODEN: JOCEAH; ISSN: 0022-3263  
 AU Chehade, Kareem A. H.; Andres, Douglas A.; Morimoto, Hiromi; Spielmann, H.  
 Peter  
 AN 2000:239015 HCAPLUS  
 DN 133:17642

L246 ANSWER 6 OF 324 MEDLINE DUPLICATE 3  
 TI Changes in **isoprenoid** lipid **synthesis** by gemfibrozil  
 and clofibric acid in rat hepatocytes.  
 SO BIOCHEMICAL PHARMACOLOGY, (2000 May 15) 59 (10) 1203-10.  
 Journal code: 0101032. ISSN: 0006-2952.  
 AU Hashimoto F; Taira S; Hayashi H  
 AN 2000202023 MEDLINE

L246 ANSWER 7 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Forskolin studies  
 SO Tetrahedron (2000), 56(8), 1081-1095  
 CODEN: TETRAB; ISSN: 0040-4020  
 AU Behnke, Dirk; Hennig, Lothar; Findeisen, Matthias; Welzel, Peter; Muller,  
 Dietrich; Thormann, Michael; Hofmann, Hans-Jorg  
 AN 2000:147117 HCAPLUS  
 DN 132:279368

L246 ANSWER 8 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 4  
 TI Biosynthesis of **carotenoids** in the chloroplasts of algae and  
 higher plants  
 SO RUSSIAN JOURNAL OF PLANT PHYSIOLOGY, (NOV-DEC 2000) Vol. 47, No. 6, pp.  
 796-814.  
 Publisher: MAIK NAUKA/INTERPERIODICA, C/O KLUWER ACADEMIC-PLENUM  
 PUBLISHERS, 233 SPRING ST, NEW YORK, NY 10013-1578.  
 ISSN: 1021-4437.  
 AU Ladygin V G (Reprint)  
 AN 2000:904268 SCISEARCH

- L246 ANSWER 9 OF 324 MEDLINE DUPLICATE 5  
 TI Metabolism of farnesyl diphosphate in tobacco BY-2 cells treated with squalenestatin.  
 SO BIOCHEMICAL SOCIETY TRANSACTIONS, (2000 Dec) 28 (6) 794-6.  
 Journal code: 7506897. ISSN: 0300-5127.  
 AU Hartmann M A; Wentzinger L; Hemmerlin A; Bach T J  
 AN 2001301221 MEDLINE
- L246 ANSWER 10 OF 324 MEDLINE DUPLICATE 6  
 TI Improving **lycopene production** in Escherichia coli by engineering metabolic control.  
 SO NATURE BIOTECHNOLOGY, (2000 May) 18 (5) 533-7.  
 Journal code: 9604648. ISSN: 1087-0156.  
 AU Farmer W R; Liao J C  
 AN 2000264176 MEDLINE
- L246 ANSWER 11 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Ethylene and glycosidase promotion in GA3- and IAA-treated tomato fruit (Lycopersicon esculentum Mill.)  
 SO Journal of Plant Growth Regulation (2000), 19(3), 359-368  
 CODEN: JPGRDI; ISSN: 0721-7595  
 AU Sozzi, G. O.; Trincherro, G. D.; Fraschina, A. A.  
 AN 2001:286480 HCAPLUS  
 DN 135:43583
- L246 ANSWER 12 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 7  
 TI Emission of volatiles from brown boronia flowers: Some comparative observations  
 SO ANNALS OF BOTANY, (AUG 2000) Vol. 86, No. 2, pp. 347-354.  
 Publisher: ACADEMIC PRESS LTD, 24-28 OVAL RD, LONDON NW1 7DX, ENGLAND.  
 ISSN: 0305-7364.  
 AU MacTavish H S (Reprint); Davies N W; Menary R C  
 AN 2000:596461 SCISEARCH
- L246 ANSWER 13 OF 324 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
 TI Protein phosphatase activity is increased in a rat model of long-term .beta.-adrenergic stimulation.  
 SO Naunyn-Schmiedeberg's Archives of Pharmacology, (2000) 362/3 (222-231).  
 Refs: 60  
 ISSN: 0028-1298 CODEN: NSAPCC  
 AU Boknik P.; Fockenbrock M.; Herzig S.; Knapp J.; Linck B.; Luss H.; Muller F.U.; Muller T.; Schmitz W.; Schroder F.; Neumann J.  
 AN 2000316049 EMBASE
- L246 ANSWER 14 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 8  
 TI Fosmidomycin as an inhibitor of the non-mevalonate terpenoid pathway depresses **synthesis** of secondary **carotenoids** in flagellates of the green alga Haematococcus pluvialis  
 SO JOURNAL OF APPLIED BOTANY-ANGEWANDTE BOTANIK, (SEP 2000) Vol. 74, No. 3-4, pp. 137-140.  
 Publisher: BLACKWELL WISSENSCHAFTS-VERLAG GMBH, KURFURSTENDAMM 57, D-10707 BERLIN, GERMANY.  
 ISSN: 0949-5460.  
 AU Hagen C (Reprint); Grunewald K  
 AN 2000:716267 SCISEARCH
- L246 ANSWER 15 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 TI Roseinatronobacter thiooxidans gen. nov., sp. nov., a new alkaliphilic aerobic bacteriochlorophyll a-containing bacterium isolated from a soda lake.  
 SO Mikrobiologiya, (Jan. Feb., 2000) Vol. 69, No. 1, pp. 89-97. print.  
 ISSN: 0026-3656.  
 AU Sorokin, D. Yu. (1); Tourova, T. P.; Kuznetsov, B. B.; Bryantseva, I. A.;

Gorlenko, V. M.  
AN 2000:384119 BIOSIS

L246 ANSWER 16 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 9  
TI Roseinatronobacter thiooxidans gen. nov., sp. nov., a new alkaliphilic  
aerobic bacteriochlorophyll a - containing bacterium isolated from a soda  
lake  
SO MICROBIOLOGY, (JAN-FEB 2000) Vol. 69, No. 1, pp. 75-82.  
Publisher: MAIK NAUKA/INTERPERIODICA, C/O PLENUM/CONSULTANTS BUREAU 233  
SPRING ST, NEW YORK, NY 10013.  
ISSN: 0026-2617.  
AU Sorokin D Y (Reprint); Tourova T P; Kuznetsov B B; Bryantseva I A;  
Gorlenko V M  
AN 2000:220386 SCISEARCH

L246 ANSWER 17 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 10  
TI Separation of chlorophylls and **carotenoids** from marine  
phytoplankton: a new HPLC method using a reversed phase C-8 column and  
pyridine-containing mobile phases  
SO MARINE ECOLOGY-PROGRESS SERIES, (APR 2000) Vol. 195, pp. 29-45.  
Publisher: INTER-RESEARCH, NORDBUNTE 23, D-21385 OLDENDORF LUHE, GERMANY.  
ISSN: 0171-8630.  
AU Zapata M (Reprint); Rodriguez F; Garrido J L  
AN 2000:340849 SCISEARCH

L246 ANSWER 18 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Application and synthesis of chloro(halo)isopentenyl **acetate**  
SO Shanghai Huagong (2000), 25(6), 11-14  
CODEN: SHAHE2; ISSN: 1004-017X  
AU Chen, Yu; Xia, Shunwei; Fu, Jiansong  
AN 2000:319928 HCAPLUS  
DN 133:176941

L246 ANSWER 19 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
TI Process for **making** metabolites of **lycopene**.  
SO Official Gazette of the United States Patent and Trademark Office Patents,  
(Dec. 28, 1999) Vol. 1229, No. 4, pp. No pagination. e-file.  
ISSN: 0098-1133.  
AU Pfander, Hanspeter (1); Traber, Bruno  
AN 2000:301644 BIOSIS

L246 ANSWER 20 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Production of paintable/bondable polymeric articles by treatment with  
oxidizing agents  
SO PCT Int. Appl., 54 pp.  
CODEN: PIXXD2  
IN Beholz, Lars Guenter  
AN 1999:626234 HCAPLUS  
DN 131:244247

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9948933	A1	19990930	WO 1999-US6270	19990324
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6077913	A	20000620	US 1998-48609	19980326
US 6100343	A	20000808	US 1998-196608	19981103
CA 2325732	AA	19990930	CA 1999-2325732	19990324
AU 9931981	A1	19991018	AU 1999-31981	19990324

L246 ANSWER 21 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Method for accelerated uptake of **carotenoid** mixtures into serum and tissues

SO PCT Int. Appl., 23 pp.

CODEN: PIXXD2

IN Tronnier, Hagen

AN 1999:626018 HCAPLUS

DN 131:248057

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9948468	A1	19990930	WO 1999-EP1661	19990313
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19812777	A1	19991007	DE 1998-19812777	19980324

L246 ANSWER 22 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Regio- and stereoselective synthesis of N-H aziridines by N-N bond reduction of N-quinazolinyl aziridines

SO Tetrahedron (1999), 55(32), 9669-9686

CODEN: TETRAB; ISSN: 0040-4020

AU Koohang, Ali; Stanchina, Corey L.; Coates, Robert M.

AN 1999:512063 HCAPLUS

DN 131:271853

L246 ANSWER 23 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISI

TI Inhibition of trichothecin and ergosterol biosynthesis in Trichothecium roseum by lovastatin

SO JOURNAL OF THE CHINESE CHEMICAL SOCIETY, (OCT 1999) Vol. 46, No. 5, pp. 687-692.

Publisher: CHINESE CHEM SOC, PO BOX 609, TAIPEI 10099, TAIWAN.

ISSN: 0009-4536.

AU Huang W L; Lee K R; Shiao M S (Reprint)

AN 1999:807008 SCISEARCH

L246 ANSWER 24 OF 324 MEDLINE DUPLICATE 11

TI Enhancement of sterol synthesis by the monoterpene perillyl alcohol is unaffected by competitive 3-hydroxy-3-methylglutaryl-CoA reductase inhibition.

SO LIPIDS, (1999 Jun) 34 (6) 605-15.

Journal code: 0060450. ISSN: 0024-4201.

AU Cerda S R; Wilkinson J 4th; Branch S K; Broitman S A

AN 1999334447 MEDLINE

L246 ANSWER 25 OF 324 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. DUPLICATE 12

TI Integration of the metabolic pathways of steroids, **carotenoids**, and retinoids.

SO Critical Reviews in Biochemistry and Molecular Biology, (1999) 34/6 (405-410).

Refs: 31

ISSN: 1040-9238 CODEN: CRBBEJ

AU Gawienowski A.M.

AN 2000037032 EMBASE

L246 ANSWER 26 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISI DUPLICATE 13

TI Atmospheric chemistry over the auyantepuy - (5 degrees 46' N; 62 degrees 32' W; 2100 meters asl)

SO INTERCIENCIA, (NOV-DEC 1999) Vol. 24, No. 6, pp. 372-380.

Publisher: INTERCIENCIA, APARTADO 51842, CARACAS 1050A, VENEZUELA.

ISSN: 0378-1844.

AU Sanhueza E (Reprint); Donoso L; Santana M; Fernandez E; Romero J

AN 2000:21195 SCISEARCH

- L246 ANSWER 27 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISI  
 TI Production of wax esters during aerobic growth of marine bacteria on **isoprenoid** compounds  
 SO APPLIED AND ENVIRONMENTAL MICROBIOLOGY, (JAN 1999) Vol. 65, No. 1, pp. 221-230.  
 Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171.  
 ISSN: 0099-2240.  
 AU Rontani J F (Reprint); Bonin P C; Volkman J K  
 AN 1999:61012 SCISEARCH
- L246 ANSWER 28 OF 324 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI  
 TI Production of astaxanthin in Haematococcus pluvialis cultured in various media;  
 the effect of culture medium composition on **carotenoid production** by an alga, for use in the food industry  
 SO Bioresource Technol.; (1999) 68, 2, 197-99  
 CODEN: BIRTEB ISSN: 0960-8524  
 AU Tripathi U; Sarada R; Rao S R; \*Ravishankar G A  
 AN 1999-04914 BIOTECHDS
- L246 ANSWER 29 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI New plasticizer EDOS for polar polymers on base of formals of dioxane alcohols  
 SO Scientific Israel--Technological Advantages (1999), 1(1), 8-15  
 CODEN: SITAFG  
 AU Gotlib, E. M.; Grinberg, L. P.; Verizhnikov, L. V.; Liakumovich, A. G.  
 AN 1999:415543 HCAPLUS  
 DN 131:215105
- L246 ANSWER 30 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Production method of adhesive tape with good adhesion  
 SO Jpn. Kokai Tokkyo Koho, 4 pp.  
 CODEN: JKXXAF  
 IN Tokuda, Kenji; Matsuki, Chikara; Shimizu, Ikusuke  
 AN 1998:334829 HCAPLUS  
 DN 129:42028
- | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|-------------|------|----------|-----------------|----------|
| JP 10140112 | A2   | 19980526 | JP 1996-304592  | 19961115 |
- L246 ANSWER 31 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
 TI Preparation of retinyl triphenylphosphonium salts.  
 PI RU 2119494 C1 19980927 (200015)\* C07F009-54  
 IN BELOVA, V M; BELOVODSKII, V P; OZOROVA, T I
- L246 ANSWER 32 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 15  
 TI 2,6-cyclolycopene-1,5-diol: Total synthesis of a naturally occurring oxidation product of **lycopene**  
 SO TETRAHEDRON, (30 JUL 1998) Vol. 54, No. 31, pp. 9011-9022.  
 Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.  
 ISSN: 0040-4020.  
 AU Traber B; Pfander H (Reprint)  
 AN 1998:551305 SCISEARCH
- L246 ANSWER 33 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI The 1-deoxy-D-xylulose-5-phosphate pathway for biosynthesis of **carotenoids** and other plastidic **isoprenoids**  
 SO Photosynthesis: Mechanisms and Effects, Proceedings of the International Congress on Photosynthesis, 11th, Budapest, Aug. 17-22, 1998 (1998), Volume 4, 3215-3220. Editor(s): Garab, Gyoza. Publisher: Kluwer Academic Publishers, Dordrecht, Neth.  
 CODEN: 68VVAS

AU Lichtenthaler, Hartmut K.; Schwender, Jorg; Muller, Christian  
AN 2000:284717 HCAPLUS  
DN 133:319495

L246 ANSWER 34 OF 324 MEDLINE DUPLICATE 16  
TI Cloning and characterization of a gene from *Escherichia coli* encoding a transketolase-like enzyme that catalyzes the synthesis of D-1-deoxyxylulose 5-phosphate, a common precursor for **isoprenoid**, thiamin, and pyridoxol biosynthesis.  
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Mar 3) 95 (5) 2105-10.  
Journal code: 7505876. ISSN: 0027-8424.  
AU Lois L M; Campos N; Putra S R; Danielsen K; Rohmer M; Boronat A  
AN 1998151473 MEDLINE

L246 ANSWER 35 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI A family of transketolases that directs **isoprenoid** biosynthesis via a mevalonate-independent pathway  
SO Proceedings of the National Academy of Sciences of the United States of America (1998), 95(5), 2100-2104  
CODEN: PNASA6; ISSN: 0027-8424  
AU Lange, B. Markus; Wildung, Mark R.; McCaskill, David; Croteau, Rodney  
AN 1998:173074 HCAPLUS  
DN 128:305603

L246 ANSWER 36 OF 324 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI  
TI Biological activities of abscisic acid analogs in the morphological change of the green alga *Haematococcus pluvialis*; for e.g. astaxanthin production  
SO J.Ferment.Bioeng.; (1998) 85, 5, 529-31  
CODEN: JFBIEX ISSN: 0922-338X  
AU Kobayashi M; Todoroki Y; Hirai N; Kurimura Y; Ohigashi H; Tsuji Y  
AN 1998-10565 BIOTECHDS

L246 ANSWER 37 OF 324 MEDLINE DUPLICATE 17  
TI Distribution of the mevalonate and glyceraldehyde phosphate/pyruvate pathways for **isoprenoid** biosynthesis in unicellular algae and the cyanobacterium *Synechocystis* PCC 6714.  
SO BIOCHEMICAL JOURNAL, (1998 Jul 15) 333 ( Pt 2) 381-8.  
Journal code: 2984726R. ISSN: 0264-6021.  
AU Disch A; Schwender J; Muller C; Lichtenthaler H K; Rohmer M  
AN 1998324900 MEDLINE

L246 ANSWER 38 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
TI On the absence of the glyceraldehyde 3-phosphate/pyruvate pathway for **isoprenoid** biosynthesis in fungi and yeasts.  
SO FEMS Microbiology Letters, (Nov. 15, 1998) Vol. 168, No. 2, pp. 201-208.  
ISSN: 0378-1097.  
AU Disch, Andrea; Rohmer, Michel (1)  
AN 1999:5130 BIOSIS

L246 ANSWER 39 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Production of astaxanthin in *Haematococcus pluvialis* cultured in various media  
SO Bioresource Technology (1998), Volume Date 1999, 68(2), 197-199  
CODEN: BIRTEB; ISSN: 0960-8524  
AU Tripathi, Usha; Sarada, R.; Rao, S. Ramachandra; Ravishankar, G. A.  
AN 1999:115935 HCAPLUS  
DN 130:222206

L246 ANSWER 40 OF 324 MEDLINE DUPLICATE 18  
TI Distribution of mevalonate and glyceraldehyde 3-phosphate/pyruvate routes for **isoprenoid** biosynthesis in some gram-negative bacteria and mycobacteria.

SO FEMS MICROBIOLOGY LETTERS, (1998 Jul 1) 164 (1) 169-75.  
Journal code: 7705721. ISSN: 0378-1097.  
AU Putra S R; Disch A; Bravo J M; Rohmer M  
AN 1998340514 MEDLINE

L246 ANSWER 41 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Study on **production** conditions of **carotenoid**  
SO Shipin Kexue (Beijing) (1998), 19(8), 20-22  
CODEN: SPKHD5; ISSN: 1002-6630  
AU Yang, Ge; Li, Ya  
AN 1998:761146 HCAPLUS  
DN 130:181535

L246 ANSWER 42 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 19  
TI Inhibition of plant growth by mevinolin and reversal of this inhibition by  
**isoprenoids**  
SO SOUTH AFRICAN JOURNAL OF BOTANY, (FEB 1998) Vol. 64, No. 1, pp. 18-24.  
Publisher: BUREAU SCIENTIFIC PUBL, P O BOX 2600, PRETORIA 0001, SOUTH  
AFRICA.  
ISSN: 0254-6299.  
AU Josekutty P C (Reprint)  
AN 1998:304704 SCISEARCH

L246 ANSWER 43 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
TI Glue composition for footwear **production** - comprises  
butadiene-nitrile rubber, chlorinated **isoprene**,  
tert-butyl-phenol formaldehyde resin, zinc and magnesium oxide(s), silica,  
and ethyl **acetate**.  
PI RU 2078108 Cl 19970427 (199805)\* 7p C09J109-02  
IN GLAGOLEV, V A; LYUSOVA, L R; NORKIN, I S

L246 ANSWER 44 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Total synthesis of C31-methyl ketone apocarotenoids 3. On the structure of  
hopkinsiaxanthin: first total synthesis of (all-E)-(3S)- and  
(9Z)-(3S)-7'-apohopkinsiaxanthin  
SO Acta Chemica Scandinavica (1997), 51(12), 1201-1216  
CODEN: ACHSE7; ISSN: 0904-213X  
AU Haugan, Jarle Andre; Lobkovsky, Emil; Liaaen-Jensen, Synnve  
AN 1997:751755 HCAPLUS  
DN 128:48384

L246 ANSWER 45 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Photobiology of the Gonyaulax circadian system. Part 2. Allopurinol  
inhibits blue-light effects  
SO Planta (1997), 202(4), 502-509  
CODEN: PLANAB; ISSN: 0032-0935  
AU Deng, Tzu Shing; Roenneberg, Till  
AN 1997:518058 HCAPLUS  
DN 127:202708

L246 ANSWER 46 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 20  
TI DIELS-ALDER REACTION OF IN-SITU GENERATED P-BENZOQUINONES WITH  
**ISOPRENOIDAL DIENOL ACETATE** - NOVEL **SYNTHESIS**  
OF 2-**ISOPRENOIDAL** NAPHTHALENE-5,8-QUINOLS  
SO TETRAHEDRON LETTERS, (28 OCT 1996) Vol. 37, No. 44, pp. 8037-8040.  
ISSN: 0040-4039.  
AU RANI A; KUMAR B; SURYAWANSHI S N (Reprint); BHAKUNI D S  
AN 96:814389 SCISEARCH

L246 ANSWER 47 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Micellization of Model Graft Copolymers of the H and .pi. Type in Dilute  
Solution  
SO Macromolecules (1996), 29(23), 7378-7385  
CODEN: MAMOBX; ISSN: 0024-9297

AU Pispas, Stergios; Hadjichristidis, Nikos; Mays, Jimmy W.  
AN 1996:623246 HCAPLUS  
DN 125:330151

L246 ANSWER 48 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 21  
TI Protein kinase C in cultured human placental trophoblasts: Identification  
of isoforms and role in cAMP signalling  
SO BIOCHEMICAL JOURNAL, (15 DEC 1996) Vol. 320, Part 3, pp. 831-836.  
Publisher: PORTLAND PRESS, 59 PORTLAND PLACE, LONDON, ENGLAND W1N 3AJ.  
ISSN: 0264-6021.  
AU Karl P I (Reprint); Divald A  
AN 97:36672 SCISEARCH

L246 ANSWER 49 OF 324 MEDLINE DUPLICATE 22  
TI Alterations in cell cholesterol content modulate Ca(2+)-induced tight  
junction assembly by MDCK cells.  
SO LIPIDS, (1996 Aug) 31 (8) 817-28.  
Journal code: 0060450. ISSN: 0024-4201.  
AU Stankewich M C; Francis S A; Vu Q U; Schneeberger E E; Lynch R D  
AN 97023524 MEDLINE

L246 ANSWER 50 OF 324 MEDLINE DUPLICATE 23  
TI Separate compartments for the **production** of sterols,  
**carotenoids** and gibberellins in *Gibberella fujikuroi*.  
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1996 Aug 1) 239 (3) 720-5.  
Journal code: 0107600. ISSN: 0014-2956.  
AU Domenech C E; Giordano W; Avalos J; Cerda-Olmedo E  
AN 96370822 MEDLINE

L246 ANSWER 51 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Carbon sources for fatty acid and sterol biosynthesis in *Leishmania*  
species  
SO Biochemical Society Transactions (1996), 24(3), 434S  
CODEN: BCSTB5; ISSN: 0300-5127  
AU Ginger, Michael L.; Chance, Michael L.; Goad, L. John  
AN 1996:570519 HCAPLUS  
DN 125:296815

L246 ANSWER 52 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Example 8: .beta.,.beta.-**carotene**  
SO Carotenoids (1996), Volume 2, 327-329. Editor(s): Britton, George;  
Liaaen-Jensen, Synnoeve; Pfander, Hanspeter. Publisher: Birkhaeuser,  
Boston, Mass.  
CODEN: 60YYAW  
AU Paust, Joachim; Manchand, Percy S.  
AN 1996:535238 HCAPLUS  
DN 125:196054

L246 ANSWER 53 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Carotenoid synthesis**. Sulfone coupling  
SO Carotenoids (1996), Volume 2, 311-314. Editor(s): Britton, George;  
Liaaen-Jensen, Synnoeve; Pfander, Hanspeter. Publisher: Birkhaeuser,  
Boston, Mass.  
CODEN: 60YYAW  
AU Otera, Junzo  
AN 1996:535234 HCAPLUS  
DN 125:222184

L246 ANSWER 54 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Thermal and NMR characterization of polysulfones prepared from 1,3 dienes  
and olefins  
SO Book of Abstracts, 211th ACS National Meeting, New Orleans, LA, March  
24-28 (1996), POLY-174 Publisher: American Chemical Society, Washington,  
D. C.



CODEN: 62PIAJ

AU Davies, Jack D.; Daly, William H.  
AN 1996:221909 HCAPLUS

L246 ANSWER 55 OF 324 MEDLINE DUPLICATE 24

TI Evidence for farnesol-mediated **isoprenoid synthesis**  
regulation in a halophilic archaeon, *Haloferax volcanii*.

SO FEBS LETTERS, (1996 Jan 22) 379 (1) 43-6.  
Journal code: 0155157. ISSN: 0014-5793.

AU Tachibana A; Tanaka T; Taniguchi M; Oi S  
AN 96159018 MEDLINE

L246 ANSWER 56 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Farnesyl compounds as cholesterol-lowering agents

SO U.S., 6 pp.  
CODEN: USXXAM

IN Bradfute, David L.; Simoni, Robert D.

AN 1996:35008 HCAPLUS

DN 124:106678

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5475029	A	19951212	US 1993-88698	19930708

L246 ANSWER 57 OF 324 WPIDS (C) 2003 THOMSON DERWENT

TI **Prodn.** of beta **carotene** in improved yield - by  
condensing retinyl-tri phenyl-phosphonic acid salt.

PI RU 2032667 Cl 19950410 (199610)\* 4p C07C403-24

IN SAMOKUVALOV, G I; VAKULOVA, L A; ZHIDKOVA, T A

L246 ANSWER 58 OF 324 MEDLINE DUPLICATE 25

TI Ubiquinone biosynthesis in *Leishmania major* promastigotes.

SO INTERNATIONAL JOURNAL FOR PARASITOLOGY, (1995 Mar) 25 (3) 279-84.  
Journal code: 0314024. ISSN: 0020-7519.

AU Ranganathan G; Mukkada A J

AN 95325056 MEDLINE

L246 ANSWER 59 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 26

TI C-15-ALLENIC MODEL COMPOUNDS FOR **CAROTENOIDS - SYNTHESIS**  
, COMPARATIVE H-1-NMR DATA AND A NEW INTRAMOLECULAR REACTION

SO ACTA CHEMICA SCANDINAVICA, (APR 1995) Vol. 49, No. 4, pp. 271-277.  
ISSN: 0904-213X.

AU HAUGAN J A (Reprint); LIAAENJENSEN S

AN 95:311339 SCISEARCH

L246 ANSWER 60 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 27

TI ENVIRONMENTAL AND DEVELOPMENTAL REGULATION OF **CAROTENOGENESIS** IN  
THE DIMORPHIC FUNGUS *MUCOR-ROUXII*

SO CURRENT MICROBIOLOGY, (SEP 1995) Vol. 31, No. 3, pp. 141-145.  
ISSN: 0343-8651.

AU MOSQUEDACANO G; GUTIERREZCORONA J F (Reprint)

AN 95:518533 SCISEARCH

L246 ANSWER 61 OF 324 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI

TI *Phaffia* strains transformed with genes encoding heterologous protein or  
**carotenoid**;

*Phaffia rhodozyma* transformation; potential in recombinant protein and  
**carotenoid** e.g. astaxanthin, zeaxanthin, cantaxanthin and  
beta-**carotene** production

AN 1994-06988 BIOTECHDS

PI WO 9406918 31 Mar 1994

L246 ANSWER 62 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI **Synthesis** of .beta.-**carotene**

SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 10 pp.

CODEN: CNXXEV

IN Zheng, Qingquan  
AN 1995:874825 HCAPLUS  
DN 123:256440

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1090271	A	19940803	CN 1993-117490	19930920

L246 ANSWER 63 OF 324 WPIDS (C) 2003 THOMSON DERWENT

TI Complex of biologically active lipids **prodn.** - with increase in **carotenoid** content by using a medium contg. sodium **acetate** and vitamin B1.

PI RU 2022019 C1 19941030 (199526)\* 4p C12P007-64  
IN FUNTIKOVA, N S; KONOVA, I V; TORLANOVA, B D

L246 ANSWER 64 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Palladium-catalyzed vinylation of tertiary allylic alcohols: a new protocol for the **synthesis** of **isoprenoid** aldehydes

SO Tetrahedron (1994), 50(11), 3389-96

CODEN: TETRAB; ISSN: 0040-4020

AU Bienayme, Hugues; Yezeguelian, Catherine

AN 1994:605716 HCAPLUS

DN 121:205716

L246 ANSWER 65 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Biosynthesis of natural products

SO Hwahak Sekye (1994), 34(11), 1056-9

CODEN: HWSEEX; ISSN: 1225-004X

AU Shin, G. H.

AN 1995:556661 HCAPLUS

DN 123:51769

L246 ANSWER 66 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI **Synthesis** of isotopically labeled **carotenoids**; investigations on structure and function of **carotenoproteins** at the atomic level

SO Pure and Applied Chemistry (1994), 66(5), 963-72

CODEN: PACHAS; ISSN: 0033-4545

AU Jansen, F. J. H. M.; Lugtenburg, J.

AN 1995:23914 HCAPLUS

DN 122:31722

L246 ANSWER 67 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISI

TI MALATE AS ADDITIONAL SUBSTRATE FOR FATTY-ACID SYNTHESIS IN A C-4-PLANT TYPE DEVELOPED BY SALT STRESS FROM A C-3-PLANT TYPE MAIZE - A SCREENING FOR MALATE AS SUBSTRATE FOR FATTY-ACID SYNTHESIS IN CHLOROPLASTS

SO JOURNAL OF PLANT PHYSIOLOGY, (MAY 1994) Vol. 143, No. 4-5, pp. 544-549. ISSN: 0176-1617.

AU PREISS M; KOOPMANN E; MEYER G; KOYRO H W; SCHULTZ G (Reprint)

AN 94:350525 SCISEARCH

L246 ANSWER 68 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 28

TI METABOLIC PATHWAY FOR BETA-CAROTENE BIOSYNTHESIS - SIMILARITIES IN THE PLANT AND ANIMAL

SO ACS SYMPOSIUM SERIES, (1994) Vol. 546, pp. 401-412.

ISSN: 0097-6156.

AU GAWIENOWSKI A M (Reprint)

AN 94:267955 SCISEARCH

L246 ANSWER 69 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 29

TI HYPER-ACCUMULATION OF ASTAXANTHIN IN A GREEN-ALGA HAEMATOCOCCUS-PLUVIALIS AT ELEVATED-TEMPERATURES

SO BIOTECHNOLOGY LETTERS, (FEB 1994) Vol. 16, No. 2, pp. 133-138.

ISSN: 0141-5492.

- AU TJAHOJONO A E (Reprint); HAYAMA Y; KAKIZONO T; TERADA Y; NISHIO N; NAGAI S  
AN 94:192033 SCISEARCH
- L246 ANSWER 70 OF 324 MEDLINE DUPLICATE 30  
TI 3-Hydroxy-3-methylglutaryl-coenzyme A reductase inhibition in a rat mast cell line. Impairment of tyrosine kinase-dependent signal transduction and the subsequent degranulation response.  
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Jul 15) 268 (20) 15252-9.  
Journal code: 2985121R. ISSN: 0021-9258.  
AU Shakarjian M P; Eiseman E; Penhallow R C; Bolen J B  
AN 93315510 MEDLINE
- L246 ANSWER 71 OF 324 MEDLINE DUPLICATE 31  
TI Family of glycosyl transferases needed for the synthesis of succinoglycan by Rhizobium meliloti.  
SO JOURNAL OF BACTERIOLOGY, (1993 Nov) 175 (21) 7033-44.  
Journal code: 2985120R. ISSN: 0021-9193.  
AU Glucksmann M A; Reuber T L; Walker G C  
AN 94042869 MEDLINE
- L246 ANSWER 72 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Carotenoids** and degraded **carotenoids**. 9.  
**Synthesis** of (S)-.alpha.-damascone  
SO Tetrahedron (1993), 49(9), 1871-8  
CODEN: TETRAB; ISSN: 0040-4020  
AU Mori, Kenji; Amaike, Masayasu; Itou, Masamichi  
AN 1993:408987 HCAPLUS  
DN 119:8987
- L246 ANSWER 73 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISI  
TI COMPETITION OF CO<sub>2</sub> AND **ACETATE** AS SUBSTRATES FOR FATTY-ACID SYNTHESIS IN IMMATURE CHLOROPLASTS OF BARLEY SEEDLINGS  
SO JOURNAL OF PLANT PHYSIOLOGY, (NOV 1993) Vol. 142, No. 5, pp. 525-530.  
ISSN: 0176-1617.  
AU PREISS M (Reprint); ROSIDI B; HOPPE P; SCHULTZ G  
AN 94:2910 SCISEARCH
- L246 ANSWER 74 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Carotenoid production** by a green alga, Haematococcus pluvialis  
SO Microbial Utilization of Renewable Resources (1993), Volume Date 1992, 8, 339-49  
CODEN: MURRE6  
AU Kobayashi, Makio; Kakizono, Toshihide; Nagai, Shiro  
AN 1994:101500 HCAPLUS  
DN 120:101500
- L246 ANSWER 75 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
TI Adhesive compsn. for fixing shoe-soles - contains polychloroprene, specified resins, silica, zinc and magnesium oxide(s), oligo-piperylene, di tert. butyl-para-cresol and organic solvent for improved strength and stability on storage.  
PI SU 1754753 A1 19920815 (199331)\* 4p C09J111-00  
IN IRKHIN, B L; PANTUKH, B I; TUKTAROVA, L A
- L246 ANSWER 76 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
TI Reagent for treatment of water-based drilling soln. - contains calcium **acetate**, obtd. as waste from thermal wood decomposition, magnesium chloride, by-product from di methyl dioxane prodn. and water.  
PI SU 1745750 A1 19920707 (199326)\* 4p C09K007-02  
IN ANGELOPULO, O K; AVAKOV, V E; BALABA, V I
- L246 ANSWER 77 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
TI Adhesive compsn. for adhesive tape **prodn.** - includes synthetic

**isoprene** rubber, glycerine ether of hydrogenated pine colophony and tetra ethoxy silane.

PI SU 1707043 A1 19920123 (199313)\* 3p C09J007-02  
IN ALEKSEENKO, A I; BUREEV, YU A; PARFENENKO, I D

L246 ANSWER 78 OF 324 WPIDS (C) 2003 THOMSON DERWENT

TI Glycerol derivs. useful as intermediates to **isoprenoid** phospholipid(s) - obtd. e.g. from chain **isoprenoid** cpds., by reaction in presence of di isopropyl ethylamine methylene chloride with di phenyl phospho chloridate.

PI JP 04257595 A 19920911 (199243)\* 7p C07C009-09  
US 5221796 A 19930622 (199326) 14p C07F009-02  
JP 2665630 B2 19971022 (199747) 7p C07F009-09  
IN MORI, H; NISHIKAWA, N

L246 ANSWER 79 OF 324 WPIDS (C) 2003 THOMSON DERWENT

TI New long chain glycerol derivs. - useful as intermediates for biocompatible **isoprenoid** phospholipid(s).

PI JP 04257544 A 19920911 (199243)\* 5p C07C069-30  
US 5221796 A 19930622 (199326) 14p C07F009-02  
JP 2670908 B2 19971029 (199748) 6p C07C069-30  
IN MORI, H; NISHIKAWA, N

L246 ANSWER 80 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISI

TI SQUALESTATIN-1, A POTENT INHIBITOR OF SQUALENE SYNTHASE, WHICH LOWERS SERUM-CHOLESTEROL INVIVO

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (15 JUN 1992) Vol. 267, No. 17, pp. 11705-11708.  
ISSN: 0021-9258.

AU BAXTER A; FITZGERALD B J; HUTSON J L; MCCARTHY A D (Reprint); MOTTERAM J M; ROSS B C; SAPRA M; SNOWDEN M A; WATSON N S; WILLIAMS R J; WRIGHT C  
AN 92:371596 SCISEARCH

L246 ANSWER 81 OF 324 MEDLINE

DUPLICATE 32

TI Dolichol: function, metabolism, and accumulation in human tissues.  
SO BIOCHEMISTRY AND CELL BIOLOGY, (1992 Jun) 70 (6) 382-4. Ref: 28  
Journal code: 8606068. ISSN: 0829-8211.

AU Carroll K K; Guthrie N; Ravi K  
AN 93080867 MEDLINE

L246 ANSWER 82 OF 324 MEDLINE

DUPLICATE 33

TI Fibrin acid derivatives: effects on the **synthesis** of **isoprenoid** lipids in cultured human lymphocytes.  
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1992 Jul 29) 1127 (2) 168-73.  
Journal code: 0217513. ISSN: 0006-3002.

AU Henry A; Allen C M; Stacpoole P W  
AN 92353119 MEDLINE

L246 ANSWER 83 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISI

TI CHOLESTEROL-BIOSYNTHESIS AND METABOLISM

SO CARDIOVASCULAR DRUGS AND THERAPY, (APR 1992) Vol. 6, No. 2, pp. 103-110.  
ISSN: 0920-3206.

AU RUSSELL D W (Reprint)  
AN 92:320939 SCISEARCH

L246 ANSWER 84 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI C50 bicyclic **carotenoids**: Sarcinaxanthin **synthesis**

SO Methods in Enzymology (1992), 213(Carotenoids, Pt. A), 75-86  
CODEN: MENZAU; ISSN: 0076-6879

AU Ferezou, J. P.  
AN 1993:192043 HCAPLUS  
DN 118:192043

L246 ANSWER 85 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

- DUPLICATE 34
- TI DIFLUFENICAN A **CAROTENOGENESIS** INHIBITOR ALSO REDUCES ACYL LIPID **SYNTHESIS**.
- SO PESTIC BIOCHEM PHYSIOL, (1992) 43 (1), 14-21.  
CODEN: PCBPBS. ISSN: 0048-3575.
- AU ASHTON I P; ABULNAJA K O; PALLETT K E; COLE D J; HARWOOD J L
- AN 1992:373062 BIOSIS
- L246 ANSWER 86 OF 324 WPIDS (C) 2003 THOMSON DERWENT
- TI Compsn. for coating of multilayer paper-like material - contains film-forming polymer, achromatic pigment, dye, by-product from **isoprene** rubber **prodn.** and solvent.
- PI SU 1668515 A1 19910807 (199222)\* 4p D21H019-66
- IN AKIM, E L; DAMASKINA, L N; RASSKAZOVA, N YA
- L246 ANSWER 87 OF 324 WPIDS (C) 2003 THOMSON DERWENT
- TI Prepn. of cycloalkenyl alkene(s) for **carotenoid synthesis** - by dehydrating e.g. pentadienyl tri methyl cyclohexanol derivs., in presence of alkali metal bromide etc..
- PI EP 454002 A 19911030 (199144)\* 6p  
R: AT BE CH DE FR GB IT LI NL
- JP 04225952 A 19920814 (199239) 5p C07C403-12
- US 5155255 A 19921013 (199244) 5p C07C403-12
- EP 454002 A3 19920506 (199330) 6p
- EP 454002 B1 19950628 (199530) DE 8p C07C403-12  
R: AT BE CH DE DK FR GB IT LI NL
- DE 59105828 G 19950803 (199536) C07C403-12
- JP 2945504 B2 19990906 (199942) 6p C07C403-12
- IN MAZZUCHELL, M; SOUKUP, M; SPURR, P; STIRTT, C; MAZZUCHELLI, M; STRITT, C
- L246 ANSWER 88 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
DUPLICATE 35
- TI A NEW PRENYLATION METHOD USING THE LITHIUM ENOLATE OF PRENAL REACTION WITH POLYUNSATURATED ALDEHYDES A SHORT ACCESS TO RETINAL.
- SO TETRAHEDRON LETT, (1991) 32 (35), 4499-4500.  
CODEN: TELEAY. ISSN: 0040-4039.
- AU DUHAMEL L; GUILLEMONT J; POIRIER J-M
- AN 1991:496993 BIOSIS
- L246 ANSWER 89 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISI
- TI A NEW PRENYLATION METHOD USING THE LITHIUM ENOLATE OF PRENAL - REACTION WITH POLYUNSATURATED ALDEHYDES - A SHORT ACCESS TO RETINAL
- SO TETRAHEDRON LETTERS, (1991) Vol. 32, No. 35, pp. 4499-4500.
- AU DUHAMEL L (Reprint); GUILLEMONT J; POIRIER J M; CHABARDES P
- AN 91:490978 SCISEARCH
- L246 ANSWER 90 OF 324 HCAPLUS COPYRIGHT 2003 ACS
- TI Stereospecific synthesis of the octaprenols WT3C4OH and WT3C3TOH
- SO Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya (1991), (10), 2333-8  
CODEN: IASKA6; ISSN: 0002-3353
- AU Grigor'eva, N. Ya.; Pinsker, O. A.; Moiseenkov, A. M.
- AN 1992:59665 HCAPLUS
- DN 116:59665
- L246 ANSWER 91 OF 324 MEDLINE DUPLICATE 36
- TI Cell-cycle-dependent, differential prenylation of proteins.
- SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1991 Sep 1) 200 (2) 579-90.  
Journal code: 0107600. ISSN: 0014-2956.
- AU Sepp-Lorenzino L; Rao S; Coleman P S
- AN 91364711 MEDLINE
- L246 ANSWER 92 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISI
- TI CELL-CYCLE-DEPENDENT, DIFFERENTIAL PRENYLATION OF PROTEINS
- SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1991) Vol. 200, No. 2, pp. 579-590.

AU SEPLORENZINO L; RAO S; COLEMAN P S (Reprint)  
AN 91:485814 SCISEARCH

L246 ANSWER 93 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
DUPLICATE 37  
TI ASTAXANTHIN PRODUCTION BY A GREEN ALGA HAEMATOCOCCUS-PLUVIALIS ACCOMPANIED  
WITH MORPHOLOGICAL CHANGES IN **ACETATE** MEDIA.  
SO J FERMENT BIOENG, (1991) 71 (5), 335-339.  
CODEN: JFBIEX. ISSN: 0922-338X.  
AU KOBAYASHI M; KAKIZONO T; NAGAI S  
AN 1991:346391 BIOSIS

L246 ANSWER 94 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISI  
TI ASTAXANTHIN PRODUCTION BY A GREEN-ALGA, HAEMATOCOCCUS-PLUVIALIS  
ACCOMPANIED WITH MORPHOLOGICAL-CHANGES IN **ACETATE** MEDIA  
SO JOURNAL OF FERMENTATION AND BIOENGINEERING, (1991) Vol. 71, No. 5, pp.  
335-339.  
AU KOBAYASHI M; KAKIZONO T; NAGAI S (Reprint)  
AN 91:319297 SCISEARCH

L246 ANSWER 95 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 38  
TI A GENE FROM THE PHOTOSYNTHETIC GENE-CLUSTER OF RHODOBACTER-SPHAEROIDES  
INDUCES TRANS-SUPPRESSION OF BACTERIOCHLOROPHYLL AND **CAROTENOID**  
LEVELS IN R-SPHAEROIDES AND R-CAPSULATUS  
SO CURRENT MICROBIOLOGY, (1991) Vol. 23, No. 5, pp. 259-263.  
AU PENFOLD R J; PEMBERTON J M (Reprint)  
AN 91:602934 SCISEARCH

L246 ANSWER 96 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
TI EVIDENCE FOR DIRECT ABA SYNTHESIS IN DUNALIELLA VOLVOCALES.  
SO CRYPTOGRAM BOT, (1991) 2 (2-3), 192-200.  
CODEN: CRBOEO.  
AU BOPP-BUHLER M-L; WABRA P; HARTUNG W; GIMMLER H  
AN 1992:101188 BIOSIS

L246 ANSWER 97 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISI  
TI CHRONIC AMINOPHYLLINE ADMINISTRATION - EFFECT ON DIAPHRAGM CONTRACTILITY  
AND FATIGUE RESISTANCE INVITRO  
SO AMERICAN REVIEW OF RESPIRATORY DISEASE, (1991) Vol. 144, No. 1, pp.  
121-125.  
AU KUEI J H (Reprint); SIECK G C  
AN 91:406309 SCISEARCH

L246 ANSWER 98 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
TI Prodn. of oxo-beta-ionone -by oxidn. of beta-ionone enol-**acetate**  
with chromium oxide soln. in sulphuric acid, in methylene chloride medium.  
PI SU 1544763 A 19900223 (199102)\*  
IN MICROPOLSK, M A; SAMOKHVALO, G I; TUTORSKAYA, O O

L246 ANSWER 99 OF 324 MEDLINE DUPLICATE 39  
TI Incorporation of squalene into rod outer segments.  
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1990 Aug 15) 265 (23) 13709-12.  
Journal code: 2985121R. ISSN: 0021-9258.  
AU Keller R K; Fliesler S J  
AN 90337983 MEDLINE

L246 ANSWER 100 OF 324 MEDLINE DUPLICATE 40  
TI Vitamin A metabolism in the human intestinal Caco-2 cell line.  
SO BIOCHEMISTRY, (1990 Dec 18) 29 (50) 11116-23.  
Journal code: 0370623. ISSN: 0006-2960.  
AU Quick T C; Ong D E  
AN 91105044 MEDLINE

L246 ANSWER 101 OF 324 HCAPLUS COPYRIGHT 2003 ACS

- TI Polyene **synthesis**. Ready construction of retinol-  
**carotene** fragments, (.+-.)-6(E)-LTB3 leukotrienes, and corticocin  
SO Journal of Organic Chemistry (1990), 55(25), 6203-14  
CODEN: JOCEAH; ISSN: 0022-3263  
AU Wenkert, Ernest; Guo, Ming; Lavilla, Rodolfo; Porter, Barry; Ramachandran,  
Kishore; Sheu, Jyh Horng  
AN 1991:6061 HCAPLUS  
DN 114:6061
- L246 ANSWER 102 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
DUPLICATE 41  
TI PLASTIDIC **ISOPRENOID SYNTHESIS** DURING CHLOROPLAST  
DEVELOPMENT CHANGE FROM METABOLIC AUTONOMY TO A DIVISION-OF-LABOR STAGE.  
SO PLANT PHYSIOL (BETHESDA), (1990) 93 (3), 1121-1127.  
CODEN: PLPHAY. ISSN: 0032-0889.  
AU HEINTZE A; GORLACH J; LEUSCHNER C; HOPPE P; HAGLESTEIN P; SCHULZE-SIEBERT  
D; SCHULTZ G  
AN 1990:430889 BIOSIS
- L246 ANSWER 103 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Plastidic **isoprenoid synthesis** changes from an  
autonomous to a division-of-labor stage during chloroplast maturation  
SO Curr. Res. Photosynth., Proc. Int. Conf. Photosynth., 8th (1990), Meeting  
Date 1989, Volume 3, 857-60. Editor(s): Baltscheffsky, Margareta.  
Publisher: Kluwer, Dordrecht, Neth.  
CODEN: 57BCAN  
AU Heintze, Adolf; Hoppe, Petra; Hagelstein, Petra; Goerlach, Joern; Schultz,  
Gernot  
AN 1991:446241 HCAPLUS  
DN 115:46241
- L246 ANSWER 104 OF 324 MEDLINE DUPLICATE 42  
TI Separation of **carotenes** on cyclodextrin-bonded phases.  
SO JOURNAL OF CHROMATOGRAPHY, (1990 JAN 19) 499 627-35.  
Journal code: 0427043. ISSN: 0021-9673.  
AU Stalcup A M; Jin H L; Armstrong D W; Mazur P; Derguini F; Nakanishi K  
AN 90216947 MEDLINE
- L246 ANSWER 105 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
DUPLICATE 43  
TI **SYNTHESIS** OF BACTERIAL C-50 **CAROTENOID** SARCINAXANTHIN.  
SO TETRAHEDRON, (1990) 46 (2), 475-486.  
CODEN: TETRAB. ISSN: 0040-4020.  
AU FERZOUZ J P; JULIA M  
AN 1990:180134 BIOSIS
- L246 ANSWER 106 OF 324 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. DUPLICATE 44  
TI Allylsilanes derived from .alpha.- and .beta.-ionone. Synthesis and  
unusual reactivity with electrophiles.  
SO Tetrahedron Letters, (1989) 30/44 (6067-6070).  
ISSN: 0040-4039 CODEN: TELEAY  
AU Azzari E.; Faggi C.; Gelsomini N.; Taddei M.  
AN 89281567 EMBASE
- L246 ANSWER 107 OF 324 MEDLINE DUPLICATE 45  
TI Hydroxymethylglutaryl coenzyme A reductase activity of adult Hymenolepis  
diminuta.  
SO JOURNAL OF PARASITOLOGY, (1989 Oct) 75 (5) 653-7.  
Journal code: 7803124. ISSN: 0022-3395.  
AU Fioravanti C F; Kim Y; Batten C L; Weaver J R  
AN 90011596 MEDLINE
- L246 ANSWER 108 OF 324 MEDLINE DUPLICATE 46  
TI Inhibitory effects of **carotenoids** and retinoids on the in vitro

- growth of rat C-6 glioma cells.
- SO PROCEEDINGS OF THE NATIONAL SCIENCE COUNCIL, REPUBLIC OF CHINA. PART B, LIFE SCIENCES, (1989 Jul) 13 (3) 176-83.  
Journal code: 8502426. ISSN: 0255-6596.
- AU Wang C J; Lin J K  
AN 90083477 MEDLINE
- L246 ANSWER 109 OF 324 HCAPLUS COPYRIGHT 2003 ACS
- TI Monoterpenoids transformation in Mentha leaves by means of distant hybridization
- SO Proc. - Int. Congr. Essent. Oils, Fragrances Flavours, 11th (1989), Volume 3, 43-8. Editor(s): Bhattacharyya, S. C.; Sen, N.; Sethi, K. L.  
Publisher: Oxford & IBH, New Delhi, India.  
CODEN: 57OQAS
- AU Nikolaev, A. G.; Pysova, M. T.; Lolla, L. V.  
AN 1992:528309 HCAPLUS  
DN 117:128309
- L246 ANSWER 110 OF 324 WPIDS (C) 2003 THOMSON DERWENT
- TI Di hydro-cyclo-citral prodn. by acid cyclising octadienyl enol ester - useful in synthesis of perfumes, steroid(s), etc..
- PI EP 255904 A 19880217 (198807)\* FR 7p  
JP 63044544 A 19880225 (198814)  
US 4800233 A 19890124 (198906) 5p  
US 4910347 A 19900320 (199017)  
EP 255904 B 19910102 (199102)  
DE 3766910 G 19910207 (199107)  
JP 2540337 B2 19961002 (199644) 5p C07C047-32
- IN SIMMONS, D P
- L246 ANSWER 111 OF 324 MEDLINE DUPLICATE 47
- TI **Isoprenoid synthesis** during the cell cycle. Studies of 3-hydroxy-3-methylglutaryl-coenzyme A synthase and reductase and **isoprenoid** labeling in cells synchronized by centrifugal elutriation.
- SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1988 Jul 25) 263 (21) 10104-10.  
Journal code: 2985121R. ISSN: 0021-9258.
- AU Maltese W A; Sheridan K M  
AN 88273097 MEDLINE
- L246 ANSWER 112 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
- TI A NUCLEAR MUTATION IN NICOTIANA-SYLVESTRIS CAUSING A THIAMIN-REVERSIBLE DEFECT IN SYNTHESIS OF CHLOROPLAST PIGMENTS.
- SO PLANT PHYSIOL (BETHESDA), (1988) 88 (3), 930-935.  
CODEN: PLPHAY. ISSN: 0032-0889.
- AU MCHALE N A; HANSON K R; ZELITCH I  
AN 1989:50772 BIOSIS
- L246 ANSWER 113 OF 324 MEDLINE DUPLICATE 48
- TI Prokaryotic hopanoids: the biosynthesis of the bacteriohopane skeleton. Formation of **isoprenic** units from two distinct **acetate** pools and a novel type of carbon/carbon linkage between a triterpene and D-ribose.
- SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1988 Aug 1) 175 (2) 405-11.  
Journal code: 0107600. ISSN: 0014-2956.
- AU Flesch G; Rohmer M  
AN 88296507 MEDLINE
- L246 ANSWER 114 OF 324 MEDLINE DUPLICATE 49
- TI **Isoprenoid** biosynthesis in a marine sponge of the Amphimedon genus: incorporation studies with [1-14C] **acetate**, [4-14C] cholesterol and [2-14C] mevalonate.
- SO COMPARATIVE BIOCHEMISTRY AND PHYSIOLOGY. B: COMPARATIVE BIOCHEMISTRY, (1988) 91 (2) 293-300.



Journal code: 2984730R. ISSN: 0305-0491.

AU Garson M J; Partali V; Liaaen-Jensen S; Stoilov I L  
AN 89064058 MEDLINE

L246 ANSWER 115 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI End-product regulation of **carotenogenesis** in *Phycomyces*  
SO Archives of Microbiology (1988), 150(3), 209-14  
CODEN: AMICCW; ISSN: 0302-8933  
AU Bejarano, Eduardo R.; Parra, Fernando; Murillo, Francisco J.;  
Cerdeira-Olmedo, Enrique  
AN 1988:566998 HCAPLUS  
DN 109:166998

L246 ANSWER 116 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
DUPLICATE 50  
TI BETA **CAROTENE SYNTHESIS** IN ISOLATED SPINACH  
CHLOROPLASTS ITS TIGHT LINKAGE TO PHOTOSYNTHETIC CARBON METABOLISM.  
SO PLANT PHYSIOL (BETHESDA), (1987) 84 (4), 1233-1237.  
CODEN: PLPHAY. ISSN: 0032-0889.  
AU SCHULZE-SIEBERT D; SCHULTZ G  
AN 1987:460672 BIOSIS

L246 ANSWER 117 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
DUPLICATE 51  
TI SUBSTRATE FLOW FROM PHOTOSYNTHETIC CARBON METABOLISM TO CHLOROPLAST  
**ISOPRENOID SYNTHESIS** IN SPINACH EVIDENCE FOR A PLASTIDIC  
PHOSPHOGLYCERATE MUTASE.  
SO Z NATURFORSCH SECT C BIOSCI, (1987) 42 (5), 570-580.  
CODEN: ZNCBDA. ISSN: 0341-0382.  
AU SCHULZE-SIEBERT D; HEINTZE A; SCHULTZ G  
AN 1987:299276 BIOSIS

L246 ANSWER 118 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
DUPLICATE 52  
TI REGULATORY INVOLVEMENT OF PLASTIDS IN THE DEVELOPMENT OF PEROXISOMAL  
ENZYMES IN THE COTYLEDONS OF MUSTARD SINAPIS-ALBA L. SEEDLINGS.  
SO J PLANT PHYSIOL, (1987) 126 (4-5), 421-436.  
CODEN: JPPHEY.  
AU BAJRACHARYA D; BERGFELD R; HATZFELD W-D; KLEIN S; SCHOPFER P  
AN 1987:214249 BIOSIS

L246 ANSWER 119 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Adverse effect of .beta.-**carotene** in diet on fertility of dairy  
cows  
SO Journal of Dairy Science (1987), 70(2), 357-66  
CODEN: JDSCAE; ISSN: 0022-0302  
AU Folman, Y.; Ascarelli, I.; Kraus, D.; Barash, H.  
AN 1987:495736 HCAPLUS  
DN 107:95736

L246 ANSWER 120 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
DUPLICATE 53  
TI FULL AUTONOMY IN **ISOPRENOID SYNTHESIS** IN SPINACH  
CHLOROPLASTS.  
SO PLANT PHYSIOL BIOCHEM (PARIS), (1987) 25 (2), 145-154.  
CODEN: PPBIEX.  
AU SCHULZE-SIEBERT D; SCHULTZ G  
AN 1988:68961 BIOSIS

L246 ANSWER 121 OF 324 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
TI Quantitative evaluation of .alpha.- and .beta.-adrenoceptor modulation of  
[3H]choline release in guinea pig superior cervical ganglia.  
SO Neuroscience Letters, (1987) 73/1 (65-70).  
CODEN: NELED5

AU Belluzzi O.; Travagli R.A.; Bonifazzi C.; Perri V.  
AN 87039580 EMBASE

L246 ANSWER 122 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Telomerization of **isoprene** with geranyl chloride and  
**synthesis** of E,E-farnesyl **acetate**  
SO Eesti NSV Teaduste Akadeemia Toimetised, Keemia (1986), 35(4), 269-74  
CODEN: ENTKDR; ISSN: 0201-8128  
AU Siirde, K.; Erm, A.; Valimae, T.; Muks, E.; Loiveke, I.; Laats, K.  
AN 1988:22058 HCAPLUS  
DN 108:22058

L246 ANSWER 123 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
TI ACID-CATALYZED CONDENSATION OF **ISOPRENE** WITH BETA ORCINALDEHYDE  
**SYNTHESIS** OF 2,2-DIMETHYLFORMYLCHROMANS AND SYNTHESIS OF 5  
METHYLBENZYLIDENE AND SESELIN DERIVATIVES.  
SO INDIAN J CHEM SECT B ORG CHEM INCL MED CHEM, (1986) 25 (1), 51-55.  
CODEN: IJSBDB. ISSN: 0376-4699.  
AU AHLUWALIA V K; GUPTA R  
AN 1986:216991 BIOSIS

L246 ANSWER 124 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
TI New cyclohexenyl alkenyl carboxylic acid - mfd. by reacting retinol or  
retinyl **acetate** in presence of tri phenyl phosphine and aq.  
hydrogen halide, then reacting with glyoxylic acid.  
PI JP 60231650 A 19851118 (198601)\* 5p  
JP 04025949 B 19920506 (199222) 5p C07C403-20

L246 ANSWER 125 OF 324 MEDLINE DUPLICATE 54  
TI Suppression of murine neuroblastoma growth in vivo by mevinolin, a  
competitive inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A reductase.  
SO JOURNAL OF CLINICAL INVESTIGATION, (1985 Nov) 76 (5) 1748-54.  
Journal code: 7802877. ISSN: 0021-9738.  
AU Maltese W A; Defendini R; Green R A; Sheridan K M; Donley D K  
AN 86034626 MEDLINE

L246 ANSWER 126 OF 324 MEDLINE DUPLICATE 55  
TI Differentiation of neuroblastoma cells induced by an inhibitor of  
mevalonate synthesis: relation of neurite outgrowth and  
acetylcholinesterase activity to changes in cell proliferation and blocked  
**isoprenoid synthesis**.  
SO JOURNAL OF CELLULAR PHYSIOLOGY, (1985 Dec) 125 (3) 540-58.  
Journal code: 0050222. ISSN: 0021-9541.  
AU Maltese W A; Sheridan K M  
AN 86059719 MEDLINE

L246 ANSWER 127 OF 324 MEDLINE DUPLICATE 56  
TI [Inhibition of the **synthesis** of **isoprenoid** compounds  
by phenol precursors of the benzoquinone ring of ubiquinone].  
Tormozhenie sinteza izoprenoidnykh soedinenii fenol'nykh  
predshestvennikami benzokhinonovogo kol'tsa ubikhinona.  
SO VOPROSY MEDITSINSKOI KHIMII, (1985 Sep-Oct) 31 (5) 121-3.  
Journal code: 0416601. ISSN: 0042-8809.  
AU Fedurov V V  
AN 86124850 MEDLINE

L246 ANSWER 128 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
TI Electronic components encapsulated in poly arylene sulphide compsn. -  
contg. hydrogenated diene-mono vinyl substd. aromatic copolymer,  
reinforcement, filler and organosilane.  
PI EP 114380 A 19840801 (198431)\* EN 29p  
R: AT BE CH DE FR GB IT LI LU NL SE  
JP 59167040 A 19840920 (198444)  
US 4514588 A 19850430 (198520)

- EP 114380 B 19880203 (198805) EN  
 R: AT BE CH DE FR GB IT LI LU NL SE  
 DE 3375620 G 19880310 (198811)  
 JP 63025503 B 19880525 (198824)  
 CA 1244173 A 19881101 (198848)  
 IN BEEVER, W H; CHILDERS, C W; SHUE, R S
- L246 ANSWER 129 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
 TI 4-Oxo-beta ionone prodn. by oxidn. of retro ionone - with oxygen, useful  
 as intermediate in **carotenoid synthesis**.  
 PI EP 101811 A 19840307 (198411)\* DE 12p  
 R: AT BE CH DE FR GB IT LI NL  
 JP 59029660 A 19840216 (198413)  
 DK 8303217 A 19840312 (198417)  
 EP 101811 B 19850918 (198538) EN  
 R: AT BE CH DE FR GB IT LI NL  
 DE 3360840 G 19851024 (198544)  
 JP 03007665 B 19910204 (199109)  
 IN LOHRI, B
- L246 ANSWER 130 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI **Synthesis** and bioassay of **isoprenoid**  
 3-alkylthio-1,1,1-trifluoro-2-propanones: potent, selective inhibitors of  
 juvenile hormone esterase  
 SO Archives of Biochemistry and Biophysics (1984), 228(2), 639-45  
 CODEN: ABBIA4; ISSN: 0003-9861  
 AU Prestwich, Glenn D.; Eng, Wai Si; Roe, R. Michael; Hammock, Bruce D.  
 AN 1984:81189 HCAPLUS  
 DN 100:81189
- L246 ANSWER 131 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 TI CIS POLY **ISOPRENE SYNTHESIS** IN GUAYULE PLANTS  
 PARTHENIUM-ARGENTATUM EXPOSED TO LOW NONFREEZING TEMPERATURES.  
 SO PLANT PHYSIOL (BETHESDA), (1984) 74 (3), 534-537.  
 CODEN: PLPHAY. ISSN: 0032-0889.  
 AU GOSS R A; BENEDICT C R; KEITHLY J H; NESSLER C L; STIPANOVIC R D  
 AN 1984:294272 BIOSIS
- L246 ANSWER 132 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Total synthesis of 3,4,3',4'-tetrahydro-.beta.,.beta.-**carotene**  
 -2,2'-dione  
 SO Acta Chemica Scandinavica, Series B: Organic Chemistry and Biochemistry  
 (1984), B38(1), 43-7  
 CODEN: ACBOCV; ISSN: 0302-4369  
 AU Aareskjold, Kaare; Liaaen-Jensen, Synnoeve  
 AN 1984:472975 HCAPLUS  
 DN 101:72975
- L246 ANSWER 133 OF 324 MEDLINE DUPLICATE 57  
 TI **Isoprene synthesis** in isolated embryonic Drosophila  
 cells. I. Sterol-deficient eukaryotic cells.  
 SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1983 Jul 10) 258 (13) 8503-11.  
 Journal code: 2985121R. ISSN: 0021-9258.  
 AU Silberkang M; Havel C M; Friend D S; McCarthy B J; Watson J A  
 AN 83238472 MEDLINE
- L246 ANSWER 134 OF 324 LIFESCI COPYRIGHT 2003 CSA DUPLICATE 58  
 TI Geranyl derivatives as inhibitors of the **carotenogenesis** in  
 Synechococcus PCC 6911 (Cyanobacteria).  
 SO Z. NATURFORSCH., SER. C., (1983) vol. 38C, no. 5-6, pp. 387-392.  
 AU Juettner, F.; Bogenschuetz, O.  
 AN 83:34106 LIFESCI
- L246 ANSWER 135 OF 324 WPIDS (C) 2003 THOMSON DERWENT

- TI Prod. of grafted copolymers as modifiers for **isoprene** rubber -  
by reaction of polyvinyl alcohol and epsilon-caprolactam in presence of  
lead **acetate**.
- PI SU 969703 A 19821101 (198335)\* 5p  
IN KHITRIN, S V; SPASSKAYA, R I; ZILBERMAN, E N
- L246 ANSWER 136 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
DUPLICATE 59
- TI THE MECHANISM OF ACTION OF A CHLOROSIS INDUCING TOXIN PRODUCED BY  
PSEUDOMONAS-PHASEOLICOLA.
- SO PLANT PHYSIOL (BETHESDA), (1982) 70 (4), 932-938.  
CODEN: PLPHAY. ISSN: 0032-0889.
- AU SMITH A G; RUBERY P H  
AN 1983:264025 BIOSIS
- L246 ANSWER 137 OF 324 MEDLINE DUPLICATE 60
- TI Nutrition and carbon metabolism of *Methanococcus voltae*.
- SO JOURNAL OF BACTERIOLOGY, (1982 Mar) 149 (3) 852-63.  
Journal code: 2985120R. ISSN: 0021-9193.
- AU Whitman W B; Ankwarda E; Wolfe R S  
AN 82142141 MEDLINE
- L246 ANSWER 138 OF 324 MEDLINE DUPLICATE 61
- TI Thylakoid membrane biogenesis in *Chlamydomonas reinhardtii* 137+. II.  
Cell-cycle variations in the synthesis and assembly of pigment.
- SO JOURNAL OF CELL BIOLOGY, (1982 May) 93 (2) 411-6.  
Journal code: 0375356. ISSN: 0021-9525.
- AU Janero D R; Barrnett R  
AN 82239545 MEDLINE
- L246 ANSWER 139 OF 324 HCAPLUS COPYRIGHT 2003 ACS
- TI Activity of several enzymes of a **carotene**- and  
macrotetrolide-producing actinomycete
- SO Mikrobiologiya (1982), 51(2), 202-5  
CODEN: MIKBA5; ISSN: 0026-3656
- AU Nefelova, M. V.; Sverdlova, A. N.  
AN 1982:213949 HCAPLUS  
DN 96:213949
- L246 ANSWER 140 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
- TI CHARACTERISTICS OF CHLOROPHYLL FORMATION IN THE GREEN ALGA GOLENKINIA.
- SO PLANT CELL PHYSIOL, (1981) 22 (6), 999-1010.  
CODEN: PCPHA5. ISSN: 0032-0781.
- AU ELLIS R; MOORE D; SHURE R  
AN 1982:175141 BIOSIS
- L246 ANSWER 141 OF 324 HCAPLUS COPYRIGHT 2003 ACS
- TI Stereoselective synthesis of solanesol and all-trans-decaprenol
- SO Journal of the Chemical Society, Perkin Transactions 1: Organic and  
Bio-Organic Chemistry (1972-1999) (1981), (3), 761-9  
CODEN: JCPRB4; ISSN: 0300-922X
- AU Sato, Kikumasa; Inoue, Seiichi; Onishi, Akira; Uchida, Nobuhiko; Minowa,  
Nobuto  
AN 1981:569537 HCAPLUS  
DN 95:169537
- L246 ANSWER 142 OF 324 HCAPLUS COPYRIGHT 2003 ACS
- TI Studies on chloroplast autonomy in terpenoid biosynthesis
- SO Berichte der Deutschen Botanischen Gesellschaft (1981), 94(1-2), 121-6  
CODEN: BEDBAP; ISSN: 0365-9631
- AU Grumbach, K. H.  
AN 1981:600627 HCAPLUS  
DN 95:200627

- L246 ANSWER 143 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
 TI Adhesive for paper or polymer film **prodn.** - from butadiene  
 -styrene and **isoprene**, rubber mixt., colophony ester,  
 chlorinated-polyethylene and paraffin aerosil and organic solvent.  
 PI SU 775115 B 19801030 (198129)\*  
 IN DUBOVITSKI, V K; LAVRINCHUK, L I; POTIEVSKAY, S A
- L246 ANSWER 144 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 TI THE BIOCHEMISTRY OF PLANTS A COMPREHENSIVE TREATISE VOL. 4. LIPIDS  
 STRUCTURE AND FUNCTION.  
 SO STUMPF, P. K. (ED.). THE BIOCHEMISTRY OF PLANTS: A COMPREHENSIVE TREATISE,  
 VOL. 4. LIPIDS: STRUCTURE AND FUNCTION. XV+693P. ACADEMIC PRESS, INC.: NEW  
 YORK, N.Y., USA; LONDON, ENGLAND. ILLUS. (1980) 0 (0), XV+693P.  
 ISBN: 0-12-675404-7.  
 AU STUMPF P K  
 AN 1981:73954 BIOSIS
- L246 ANSWER 145 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 DUPLICATE 62  
 TI **SYNTHESIS** OF OPTICALLY ACTIVE NATURAL **CAROTENOIDS** AND  
 STRUCTURALLY RELATED COMPOUNDS 6. **SYNTHESIS** OF PICRO CROCIN.  
 SO HELV CHIM ACTA, (1980) 63 (6), 1463-1466.  
 CODEN: HCACAV. ISSN: 0018-019X.  
 AU MAYER H; SANTER J-M  
 AN 1981:185187 BIOSIS
- L246 ANSWER 146 OF 324 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
 TI A comparison of transition metal and non-transition metal oligomerizations  
 of **isoprene** for the **synthesis** of terpenes.  
 SO Annals of the New York Academy of Sciences, (1980) VOL. 333/- (286-301).  
 CODEN: ANYAA  
 AU Chalk A.J.; Magennis S.A.  
 AN 81067868 EMBASE
- L246 ANSWER 147 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Use of the reverse osmosis method for purifying **isoprene**  
**production** wastewater  
 SO Khimicheskaya Promyshlennost (Moscow, Russian Federation) (1980), (2),  
 124-5  
 CODEN: KPRMAW; ISSN: 0023-110X  
 AU Galutkina, K. A.; Nemchenko, A. G.; Apostolova, I. V.; Karazeeva, L. N.  
 AN 1980:573093 HCAPLUS  
 DN 93:173093
- L246 ANSWER 148 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI E-4-Acetoxy-2-methyl-2-butenal  
 SO U.S., 6 pp.  
 CODEN: USXXAM  
 IN Babler, James H.  
 AN 1980:93898 HCAPLUS  
 DN 92:93898
- | PATENT NO.            | KIND | DATE     | APPLICATION NO. | DATE     |
|-----------------------|------|----------|-----------------|----------|
| US 4175204            | A    | 19791120 | US 1979-1075    | 19790108 |
| WO 7900485            | A1   | 19790726 | WO 1979-US28    | 19790116 |
| W: CH, DE, GB, JP, SE |      |          |                 |          |
| RW: CH, DE, FR, GB    |      |          |                 |          |
| EP 8581               | A1   | 19800305 | EP 1979-900203  | 19790116 |
| R: CH, DE, FR, GB     |      |          |                 |          |
- L246 ANSWER 149 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI **Synthesis** of compounds containing the **isoprene** unit.  
 A new stereoselective **synthesis** of all-trans vitamin A and of  
 methyl (2E,4E)-3,7,11-trimethyldodeca-2,4-dienoate

- SO Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1979), (7), 1729-33  
CODEN: JCPRB4; ISSN: 0300-922X  
AU Cardillo, Giuliana; Contento, Michele; Sandri, Sergio; Panunzio, Mauro  
AN 1980:94599 HCAPLUS  
DN 92:94599
- L246 ANSWER 150 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Evidence for the existence of two .beta.-**carotene** pools and two biosynthetic .beta.-**carotene** pathways in the chloroplast  
SO Zeitschrift fuer Naturforschung, C: Journal of Biosciences (1979), 34C(12), 1205-8  
CODEN: ZNCBDA; ISSN: 0341-0382  
AU Grumbach, K. H.  
AN 1980:107386 HCAPLUS  
DN 92:107386
- L246 ANSWER 151 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI The effect of PS II herbicides, amitrol and SAN 6706 on the activity of 3-hydroxy-3-methylglutaryl-coenzyme-A-reductase and the incorporation of [2-14C]-**acetate** and [2-3H]-mevalonate into chloroplast pigments of radish seedlings  
SO Zeitschrift fuer Naturforschung, C: Journal of Biosciences (1979), 34C(11), 941-3  
CODEN: ZNCBDA; ISSN: 0341-0382  
AU Grumbach, K. H.; Bach, T. J.  
AN 1980:19002 HCAPLUS  
DN 92:19002
- L246 ANSWER 152 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Effect of organic substrates on chlorophyll and **carotenoid production** of Anabaena sp. under light and dark conditions  
SO Journal of the Indian Botanical Society (1979), 58(4), 358-62  
CODEN: JIBSAC; ISSN: 0019-4468  
AU Sahu, J. K.; Adhikary, S. P.; Pattnaik, H.  
AN 1981:27160 HCAPLUS  
DN 94:27160
- L246 ANSWER 153 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
TI LIPID SYNTHESIS IN IMBIBED SPORES OF THE FERN ANEMIA-PHYLLITIDIS.  
SO Z PFLANZENPHYSIOL, (1979) 91 (4), 317-324.  
CODEN: ZSPPAD. ISSN: 0044-328X.  
AU GEMMRICH A R  
AN 1979:254296 BIOSIS
- L246 ANSWER 154 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI The role of retinol in the initiation of sporangiophores of Phycomyces blakesleeanus  
SO Planta (1979), 146(3), 257-62  
CODEN: PLANAB; ISSN: 0032-0935  
AU Galland, P.; Russo, V. E. A.  
AN 1979:554387 HCAPLUS  
DN 91:154387
- L246 ANSWER 155 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Biosynthesis of **carotene** by the yeast Sporobolomyces pararoseus T during cultivation on peat oxidate  
SO Prikladnaya Biokhimiya i Mikrobiologiya (1979), 15(2), 222-6  
CODEN: PBMIAC; ISSN: 0555-1099  
AU Koroleva, I. F.; Zalashko, M. V.; Demina, S. G.; Kosonogova, L. V.; Evdokimova, G. A.  
AN 1979:402302 HCAPLUS  
DN 91:2302

- L246 ANSWER 156 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
DUPLICATE 63
- TI **CAROTENOID** AND STEROID **SYNTHESES** BY CARROT CELLS IN  
SUSPENSION CULTURE.
- SO PHYSIOL PLANT, (1979) 46 (2), 127-132.  
CODEN: PHPLAI. ISSN: 0031-9317.
- AU SHIMIZU K; KIKUCHI T; SUGANO N; NISHI A  
AN 1979:260872 BIOSIS
- L246 ANSWER 157 OF 324 HCAPLUS COPYRIGHT 2003 ACS
- TI Selection of a nutrient medium for the production of *Rhodotorula gracilis*  
K-1 with vitamin A activity
- SO Izvestiya Akademii Nauk Moldavskoi SSR, Biologicheskie i Khimicheskie  
Nauki (1979), (3), 56-60  
CODEN: IMBKB6; ISSN: 0568-5192
- AU Atamanyuk, D. I.; Borisova, T. A.; Tsygulya, T. E.; Garkavenko, A. I.  
AN 1979:522112 HCAPLUS  
DN 91:122112
- L246 ANSWER 158 OF 324 HCAPLUS COPYRIGHT 2003 ACS
- TI Metal-assisted terpenoid **synthesis**. V. The catalytic  
trimerization of **isoprene** to trans-.beta.-farnesene and its  
synthetic applications for terpenoids
- SO Bulletin of the Chemical Society of Japan (1978), 51(4), 1158-62  
CODEN: BCSJA8; ISSN: 0009-2673
- AU Akutagawa, Susumu; Taketomi, Takanao; Kumobayashi, Hidenori; Takayama,  
Kiyoshi; Someya, Taichi; Otsuka, Sei  
AN 1978:443834 HCAPLUS  
DN 89:43834
- L246 ANSWER 159 OF 324 HCAPLUS COPYRIGHT 2003 ACS
- TI Identification of oxygen-containing organic substances from  
chromatographic spectra
- SO Zhurnal Analiticheskoi Khimii (1978), 33(4), 775-81  
CODEN: ZAKHA8; ISSN: 0044-4502
- AU Vigdergauz, M. S.; Gizzatullin, R. R.; Tukmanov, R. G.; Fedin, Yu. I.;  
Kiyanenko, G. V.  
AN 1978:484360 HCAPLUS  
DN 89:84360
- L246 ANSWER 160 OF 324 MEDLINE
- TI [Effect of organic acids on the biosynthesis of macrotetralide antibiotics  
by an *Actinomyces chrysomallus* var. **carotenoides** strain].  
Vliianie organicheskikh kislot na biosintez **makrotetralidnykh**  
antibiotikov shtammom *Actinomyces chrysomallus* var. **carotenoides**
- SO ANTIBIOTIKI, (1978 Jul) 23 (7) 586-90.  
Journal code: 0375020. ISSN: 0003-5637.
- AU Nefelova M V; Sverdlova A N; Silaev A B  
AN 78234086 MEDLINE
- L246 ANSWER 161 OF 324 HCAPLUS COPYRIGHT 2003 ACS
- TI Effect of organic acids on the biosynthesis of **carotenes** by  
*Actinomyces chrysomallus* strains
- SO Mikrobiologiya (1978), 47(2), 208-11  
CODEN: MIKBA5; ISSN: 0026-3656
- AU Nefelova, M. V.; Sverdlova, A. N.; Alekseeva, L. N.  
AN 1978:419961 HCAPLUS  
DN 89:19961
- L246 ANSWER 162 OF 324 WPIDS (C) 2003 THOMSON DERWENT
- TI Water soluble vinyl **-acetate** copolymer for fibres **prodn**  
. - by copolymerisation with **isoprene** in presence of initiator.
- PI SU 567729 A 19770831 (197824)\*

- IN GABRIELIAN, G A; PAKHOMOVA, A S; ROGOVIN, Z A
- L246 ANSWER 163 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
TI Symmetrical **carotenoids** prodn. - by reacting ylid  
cpds. with peroxy acids or their salts or esters.  
PI DE 2702633 A 19770728 (197731)\*  
DE 2702633 C 19841025 (198444)
- L246 ANSWER 164 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
DUPLICATE 64  
TI ON THE INFLUENCE OF CHOLESTEROL FEEDING AND OF A LIPOGENIC DIET ON THE  
CHOLESTEROGENESIS IN RAT LIVER IN-VIVO.  
SO HELV CHIM ACTA, (1977 (RECD 1978)) 60 (8), 2686-2694.  
CODEN: HCACAV. ISSN: 0018-019X.  
AU WISS O; WISS V  
AN 1978:234974 BIOSIS
- L246 ANSWER 165 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
DUPLICATE 65  
TI ON METABOLIC DEGRADATIONS OF SQUALENE LANOSTEROL AND CHOLESTEROL IN RAT  
LIVER IN-VIVO EVIDENCE FOR RE CYCLING OF METABOLITES FOR THE  
**SYNTHESIS** OF **ISOPRENE** COMPOUNDS.  
SO HELV CHIM ACTA, (1977) 60 (6), 1961-1966.  
CODEN: HCACAV. ISSN: 0018-019X.  
AU WISS O; WISS V  
AN 1978:157927 BIOSIS
- L246 ANSWER 166 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Hydroperoxide oxidation of phosphorus ylides: a new and useful route to  
symmetrical **carotenoids**  
SO Justus Liebigs Annalen der Chemie (1977), (7), 1146-59  
CODEN: JLACBF; ISSN: 0075-4617  
AU Nuerrenbach, Axel; Paust, Joachim; Pommer, Horst; Schneider, Joachim;  
Schulz, Bernhard  
AN 1978:121450 HCAPLUS  
DN 88:121450
- L246 ANSWER 167 OF 324 MEDLINE DUPLICATE 66  
TI [Participation of **acetate** in the biosynthesis of  
**carotenoids** and macrotetralids by Actinomyces chrysomallus var.  
**carotenoides**].  
Uchastie atsetata v biosinteze karotinoidov i **makrotetralidov**  
Actinomyces chrysomallus var. **carotenoides**.  
SO MIKROBIOLOGIYA, (1977 Nov-Dec) 46 (6) 1122-3.  
Journal code: 0376652. ISSN: 0026-3656.  
AU Sverdlova A N; Silaev A B; Alekseeva L N; Nefelova M V  
AN 78091762 MEDLINE
- L246 ANSWER 168 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
TI PARTICIPATION OF **ACETATE** IN BIOSYNTHESIS OF **CAROTENOIDS**  
AND MACRO TETRALIDES BY ACTINOMYCES-CHRYSMALLUS-VAR-**CAROTENOIDES**  
SO MIKROBIOLOGIYA, (1977 (RECD 1978)) 44 (6), 1122-1123.  
CODEN: MIKBA5. ISSN: 0026-3656.  
AU SVERDLOVA A N; SILAEV A B; ALEKSEEVA L N; NEFELOVA M V  
AN 1978:204223 BIOSIS
- L246 ANSWER 169 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Higher **isoprenoids**. V. Partial **syntheses** from  
cycloartenol, cyclolaudenol. Part 1. Mangiferolic acid, ambolic acid  
SO Tetrahedron (1977), 33(7), 817-19  
CODEN: TETRAB; ISSN: 0040-4020  
AU Singh, Chandan; Dev, Sukh  
AN 1977:536027 HCAPLUS



DN 87:136027

L246 ANSWER 170 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Total **synthesis** of dl-.alpha.-tocopherol from **isoprene**

SO Eesti NSV Teaduste Akadeemia Toimetised, Keemia, Geoloogia (1977), 26(4), 271-4

CODEN: EKEGAI; ISSN: 0424-6373

AU Laats, K.; Kogerman, A.; Ammon, K.

AN 1978:136801 HCAPLUS

DN 88:136801

L246 ANSWER 171 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Optically active cyclohexane derivatives

SO Ger. Offen., 68 pp.

CODEN: GWXXBX

IN Boguth, Walter; Leuenberger, Hans G. W.; Mayer, Hans Johann; Widmer, Erich; Zell, Reinhard

AN 1976:492200 HCAPLUS

DN 85:92200

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2537060	A1	19760304	DE 1975-2537060	19750820
DE 2537060	B2	19790523		
DE 2537060	C3	19800117		
CH 605533	A	19780929	CH 1974-11434	19740821
US 3988205	A	19761026	US 1975-601770	19750804
JP 51082789	A2	19760720	JP 1975-99888	19750819
JP 58007277	B4	19830209		
FR 2303797	A1	19761008	FR 1975-25631	19750819
FR 2303797	B1	19800725		
BE 832565	A1	19760220	BE 1975-159309	19750820
GB 1508195	A	19780419	GB 1975-34605	19750820
GB 1508197	A	19780419	GB 1976-47891	19750820
GB 1508196	A	19780419	GB 1976-47892	19750820
AT 7506455	A	19780515	AT 1975-6455	19750820
AT 347422	B	19781227		
NL 7509925	A	19760224	NL 1975-9925	19750821
NL 169195	B	19820118		
NL 169195	C	19820616		
JP 57011300	B4	19820303	JP 1976-452	19760101
FR 2303786	A1	19761008	FR 1976-16821	19760603
FR 2303786	B1	19800530		
FR 2303798	A1	19761008	FR 1976-16822	19760603
FR 2303798	B1	19821029		
US 4026949	A	19770531	US 1976-707128	19760720
US 4072715	A	19780207	US 1976-707123	19760720
US 4095038	A	19780613	US 1976-707146	19760720
US 4156100	A	19790522	US 1977-849138	19771107
JP 55033463	A2	19800308	JP 1979-66908	19790531
JP 59001692	B4	19840113		

L246 ANSWER 172 OF 324 WPIDS (C) 2003 THOMSON DERWENT

TI 4-Chloro 2-methyl crotonaldehyde **prodn.** - by chlorinating **isoprene** monoxide e.g. with tert. butyl hypochlorite, useful as vitamin A intermediate.

PI DE 2620968 A 19761118 (197648)\*  
US 4054608 A 19771018 (197743)  
DE 2620968 B 19790607 (197924)  
IT 1038011 B 19791120 (198010)

L246 ANSWER 173 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Cyclobutene derivatives as **isoprene** equivalents in terpene **synthesis**. The metathesis of 1-methylcyclobutene

SO Journal of Organic Chemistry (1976), 41(24), 3928-9

CODEN: JOCEAH; ISSN: 0022-3263

AU Wilson, Stephen R.; Schalk, David E.  
AN 1976:592924 HCAPLUS  
DN 85:192924

L246 ANSWER 174 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI New C5-compounds for terpene synthesis. I. Monoacetals of  
2-methyl-2-butene-1,4-dial  
SO Justus Liebigs Annalen der Chemie (1976), (12), 2194-205  
CODEN: JLACBF; ISSN: 0075-4617  
AU Paust, Joachim; Reif, Werner; Schumacher, Horst  
AN 1977:121562 HCAPLUS  
DN 86:121562

L246 ANSWER 175 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Bacterial **carotenoids**. II. C50-**carotenoids**. 17.  
Total **synthesis** of two bacterioruberin derivatives. Absolute  
configuration of bacterioruberin  
SO Tetrahedron Letters (1976), (12), 955-8  
CODEN: TELEAY; ISSN: 0040-4039  
AU Johansen, Jon E.; Liaaen-Jensen, Synnove  
AN 1976:446887 HCAPLUS  
DN 85:46887

L246 ANSWER 176 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI The synthesis of 2,2'-dinorcarotenoids  
SO Helvetica Chimica Acta (1976), 59(2), 439-52  
CODEN: HCACAV; ISSN: 0018-019X  
AU Kienzle, Frank; Minder, Rudolf E.  
AN 1976:421660 HCAPLUS  
DN 85:21660

L246 ANSWER 177 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
TI 2,2,6-Trimethyl-cyclohex-5-en-1,4-dione prodn - in good yields by liq  
phase catalytic oxidn of 3,3,5-trimethyl-cyclohex-4-en-1-one.  
PI DE 2457157 A 19750612 (197525)\*  
NL 7415846 A 19750610 (197526)  
JP 50093946 A 19750726 (197538)  
FR 2253730 A 19750808 (197539)  
GB 1429120 A 19760324 (197613)  
US 4010205 A 19770301 (197710)  
CH 585168 A 19770228 (197716)  
US 4026948 A 19770531 (197723)  
DE 2457157 B 19780209 (197807)  
JP 53028907 B 19780817 (197837)

L246 ANSWER 178 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Carotenoid synthesis** using sulfones.  
**Synthesis** of apocarotenoids and a torularhodin ester  
SO Helvetica Chimica Acta (1975), 58(5), 1492-7  
CODEN: HCACAV; ISSN: 0018-019X  
AU Fischli, Albert; Mayer, Hans  
AN 1975:514676 HCAPLUS  
DN 83:114676

L246 ANSWER 179 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Synthesis** and reactions of **isoprenyl** terminal epoxides  
in the chromone and quinoline series  
SO Journal of the Chemical Society, Perkin Transactions 1: Organic and  
Bio-Organic Chemistry (1972-1999) (1975), (2), 150-4  
CODEN: JCPRB4; ISSN: 0300-922X  
AU Grundon, Michael F.; Okely, H. Martyn  
AN 1975:170584 HCAPLUS  
DN 82:170584

- L246 ANSWER 180 OF 324 MEDLINE  
 TI Morphology and physiology of *Spirochaeta aurantia* strains isolated from aquatic habitats.  
 SO ARCHIVES OF MICROBIOLOGY, (1975 Sep 30) 105 (1) 1-12.  
 Journal code: 0410427. ISSN: 0302-8933.  
 AU Breznak J A; Canale-Parola E  
 AN 76060756 MEDLINE
- L246 ANSWER 181 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
 TI Pivalic acid prepn from **isoprene** - by reaction with water vapour using phosphoric acid catalyst, then oxidn of pivalaldehyde.  
 PI JP 49024895 B 19740626 (197429)\*
- L246 ANSWER 182 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
 TI **Isoprene** prepn from tert. butanol deriv - and formaldehyde using boron trifl-uoride catalyst.  
 PI JP 49010927 B 19740313 (197415)\*
- L246 ANSWER 183 OF 324 SCISEARCH COPYRIGHT 2003 THOMSON ISI  
 TI **SYNTHESES OF ISOPRENE AND ITS INTERMEDIATES FROM 3-HYDROXY-3-METHYLBUTYL ACETATE**  
 SO NIPPON KAGAKU KAISHI, (1974) Vol. 1974, No. 10, pp. 2014-2016.  
 AU FUKUNISHI.K (Reprint); NAITO I; MASHIO F  
 AN 74:352428 SCISEARCH
- L246 ANSWER 184 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI **Syntheses of isoprene and its intermediates from 3-hydroxy-3-methylbutyl acetate**  
 SO Nippon Kagaku Kaishi (1974), (10), 2014-16  
 CODEN: NKAKB8; ISSN: 0369-4577  
 AU Fukunishi, Koushi; Naito, Ikuo; Mashio, Fujio  
 AN 1975:44605 HCAPLUS  
 DN 82:44605
- L246 ANSWER 185 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI **Synthesis of partially hydrogenated isoprene dimers**  
 SO Nippon Kagaku Kaishi (1974), (9), 1677-81  
 CODEN: NKAKB8; ISSN: 0369-4577  
 AU Imaizumi, Fumitake; Ando, Naoki; Hirayanagi, Shigetoshi; Mori, Kan  
 AN 1975:18258 HCAPLUS  
 DN 82:18258
- L246 ANSWER 186 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Stereoselective coupling reactions of allylnickel complexes  
 SO Gazzetta Chimica Italiana (1974), 104(5-6), 557-66  
 CODEN: GCITA9; ISSN: 0016-5603  
 AU Guerrieri, Franco; Chiusoli, Gian P.; Merzoni, Sergio  
 AN 1974:536288 HCAPLUS  
 DN 81:136288
- L246 ANSWER 187 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Properties of *Thiocapsa roseopersicina* strain BBS isolated from the estuary of the White Sea  
 SO Mikrobiologiya (1974), 43(2), 326-32  
 CODEN: MIKBA5; ISSN: 0026-3656  
 AU Bogorov, L. V.  
 AN 1974:487746 HCAPLUS  
 DN 81:87746
- L246 ANSWER 188 OF 324 MEDLINE DUPLICATE 67  
 TI Nitrogen metabolism control of the **acetate**--stimulated **carotenoid synthesis** in *Rhodotorula sanneii*.  
 SO ZENTRALBLATT FUR BAKTERIOLOGIE, PARASITENKUNDE, INFektionsKRANKHEITEN UND

HYGIENE. ZWEITE NATURWISSENSCHAFTLICHE ABT.: ALLGEMEINE,  
LANDWIRTSCHAFTLICHE UND TECHNISCHE MIKROBIOLOGIE, (1974) 129 (1) 68-71.  
Journal code: 0414371. ISSN: 0044-4057.

AU Vuori A T; Gyllenberg H G  
AN 74304966 MEDLINE

L246 ANSWER 189 OF 324 WPIDS (C) 2003 THOMSON DERWENT  
TI 3-Methylbutanediol-1,3 prodn - by catalytic oxidn. of isoamyl  
**acetate**, hydrogenation and saponification.  
PI SU 393261 A 19731228 (197421)\*

L246 ANSWER 190 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Carotenoids** and degraded **carotenoids**. II.  
**Synthesis** of dl-3-hydroxydihydro-.beta.-damascone and  
dihydro-.beta.-damascone  
SO Agricultural and Biological Chemistry (1973), 37(12), 2907-11  
CODEN: ABCHA6; ISSN: 0002-1369  
AU Mori, Kenji; Ohki, Masahiko; Okada, Katsuhide; Takei, Yoko; Matsui,  
Masanao  
AN 1974:83309 HCAPLUS  
DN 80:83309

L246 ANSWER 191 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Synthesis of trans-4-amino-1-hydroxy-2-methyl-2-butene from  
**isoprene** (**synthesis** of zeatin)  
SO Nippon Nogei Kagaku Kaishi (1973), 47(12), 807-11  
CODEN: NNKKA; ISSN: 0002-1407  
AU Ohsugi, Motoyoshi; Takahashi, Satoru; Ichimoto, Itsuo; Ueda, Hiroo  
AN 1974:403280 HCAPLUS  
DN 81:3280

L246 ANSWER 192 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Use of microbial **carotene** in rations of two generations of hens  
in comparison with other vitamin A sources  
SO Vitam. Pitan. S-kh. Zhivotn. (1973), 286-98. Editor(s): Tomme, M. F.  
Publisher: "Kolos", Moscow, USSR.  
CODEN: 29SJA8  
AU Semin, V. N.; Tkachev, I. F.; Bukhtiyarova, O. N.  
AN 1975:407774 HCAPLUS  
DN 83:7774

L246 ANSWER 193 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Reactions of .pi.-allylic nickel(II) bromide with organic halides. Novel  
synthesis of monoterpenoid compounds  
SO Journal of Organic Chemistry (1972), 37(3), 462-6  
CODEN: JOCEAH; ISSN: 0022-3263  
AU Sato, Kikumasa; Inoue, Seichi; Ota, Satoshi; Fujita, Yoshiji  
AN 1972:85936 HCAPLUS  
DN 76:85936

L246 ANSWER 194 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Extension of shelf life of fresh fruits and vegetables. VIII. Effect of  
packaging in polyethylene bags on incorporation of 2-14C-mevalonic acid  
and 2-14C-**acetate** into tomato **carotenoids**  
SO Journal of the Japanese Society for Horticultural Science (1972), 41(1),  
92-7  
CODEN: EGKZA9; ISSN: 0013-7626  
AU Okubo, Masutaro; Umeda, Keiji  
AN 1972:486729 HCAPLUS  
DN 77:86729

L246 ANSWER 195 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Effect of potassium and sodium acetates on pigment production in  
Staphylococcus aureus 209-P

SO Mikrobiologiya (1971), 40(6), 1112-13  
CODEN: MIKBA5; ISSN: 0026-3656  
AU Ignatov, V. V.; Stupnikova, S. K.; Volkova, V. V.  
AN 1972:122238 HCAPLUS  
DN 76:122238

L246 ANSWER 196 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Effects of beta-**carotene**, vitamin A, and glucocorticoids on  
collagen synthesis in wounds  
SO Proceedings of the Society for Experimental Biology and Medicine (1971),  
137(3), 936-8  
CODEN: PSEBAA; ISSN: 0037-9727  
AU Ehrlich, H. Paul; Tarver, H.  
AN 1971:461125 HCAPLUS  
DN 75:61125

L246 ANSWER 197 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
TI **CAROTENOID SYNTHESIS** IN A SUSPENSION CULTURE OF  
CARROT-D CELLS.  
SO PLANT CELL PHYSIOL, (1971) 12 (4), 525-531.  
CODEN: PCPHA5. ISSN: 0032-0781.  
AU SUGANO N; MIYA S; NISHI A  
AN 1972:139862 BIOSIS

L246 ANSWER 198 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Regulation of the synthesis of metabolites synthesized via acetyl-coenzyme  
A in a culture of Streptomyces erythraeus  
SO Mikrobiologiya (1971), 40(2), 246-51  
CODEN: MIKBA5; ISSN: 0026-3656  
AU Bezborodov, A. M.; Galynkin, V. A.  
AN 1971:431601 HCAPLUS  
DN 75:31601

L246 ANSWER 199 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Research, conducted at the All-Union Scientific-Research Institute of  
Synthetic Rubber, on the preparation of basic monomers for the synthesis  
of rubbers  
SO Kauchuk i Rezina (1971), 30(2), 15-17  
CODEN: KCRZAE; ISSN: 0022-9466  
AU Gorin, Yu. A.  
AN 1971:143011 HCAPLUS  
DN 74:143011

L246 ANSWER 200 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Nonconjugated dienes  
SO Jpn. Tokkyo Koho, 2 pp.  
CODEN: JAXXAD  
IN Hata, Go; Aoki, Kazumi  
AN 1972:15566 HCAPLUS  
DN 76:15566

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI JP 45007526	B4	19700316	JP	19650809

L246 ANSWER 201 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Utilization of malonyl-CoA for the biosynthesis of .beta.-**carotene**  
and ergosterol in cell-free preparations from Blakeslea trispora  
SO Acta Chemica Scandinavica (1947-1973) (1970), 24(7), 2361-5  
CODEN: ACSAA4; ISSN: 0001-5393  
AU Neujahr, Halina Y.; Bjork, Lars  
AN 1971:60949 HCAPLUS  
DN 74:60949

L246 ANSWER 202 OF 324 HCAPLUS COPYRIGHT 2003 ACS

- TI Structure and **synthesis** of new phenolic **carotenoids**  
from *Streptomyces mediolani*  
SO Gazzetta Chimica Italiana (1970), 100(6), 581-90  
CODEN: GCITA9; ISSN: 0016-5603  
AU Arcamone, Federico; Cameron, Bruno; Franceschi, Giovanni; Penco, Sergio  
AN 1971:23040 HCAPLUS  
DN 74:23040
- L246 ANSWER 203 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Anaerobic growth of purple nonsulfur bacteria under dark conditions  
SO Journal of Bacteriology (1970), 104(1), 462-72  
CODEN: JOBAA; ISSN: 0021-9193  
AU Uffen, Robert L.; Wolfe, Ralph S.  
AN 1970:517618 HCAPLUS  
DN 73:117618
- L246 ANSWER 204 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
TI BIOCHEMICAL ASPECTS OF FUNGAL DIFFERENTIATION NEUROSPORA MODEL.  
SO PHYSIOL VEG, (1970) 8 (3), 375-386.  
CODEN: PHYVAP. ISSN: 0031-9368.  
AU TURIAN G  
AN 1971:147220 BIOSIS
- L246 ANSWER 205 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Reagent for the detection of acetylene derivatives on thin-layer plates  
SO Journal of Chromatography (1970), 49(2), 317-22  
CODEN: JOCRAM; ISSN: 0021-9673  
AU Schulte, Karl E.; Ruecker, G.  
AN 1970:484464 HCAPLUS  
DN 73:84464
- L246 ANSWER 206 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Use of a polarographic method in controlling vitamin production  
SO Problemy Analiticheskoi Khimii (1970), 1, 177-84  
CODEN: PYAKAP; ISSN: 0370-2677  
AU Devyatnin, V. A.; Solunina, I. A.  
AN 1971:146292 HCAPLUS  
DN 74:146292
- L246 ANSWER 207 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Catalytic ene **synthesis** with carbonyl compounds. Addition of  
**isoprene** to formaldehyde  
SO Doklady Akademii Nauk SSSR (1970), 190(1), 102-3 [Chem]  
CODEN: DANKAS; ISSN: 0002-3264  
AU Klimova, E. I.; Arbuzov, Yu. A.  
AN 1970:111143 HCAPLUS  
DN 72:111143
- L246 ANSWER 208 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Effectiveness of various sources of vitamin A in poultry rations  
SO Vestnik Sel'skokhozyaistvennoi Nauki (Moscow) (1970), 15(9), 73-82  
CODEN: VSNLAF; ISSN: 0206-6335  
AU Tkachev, I. F.; Semin, V. N.; Bukhtiyarova, O. N.  
AN 1971:10902 HCAPLUS  
DN 74:10902
- L246 ANSWER 209 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Catalytic oxidative dehydrogenation reaction of hydrocarbons. III.  
**Production of isoprene** by oxidative dehydrogenation  
SO Kogyo Kagaku Zasshi (1969), 72(12), 2571-7  
CODEN: KGKZA7; ISSN: 0368-5462  
AU Nishikawa, Eiichiro; Ueki, Toru; Mori, Goichi; Morita, Yoshiro  
AN 1970:99910 HCAPLUS  
DN 72:99910

- L246 ANSWER 210 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Biosynthesis of .beta.-**carotene** by cell-free extracts of  
Phycomyces blakesleeianus  
SO Journal of Biological Chemistry (1969), 237, 681-6  
CODEN: JBCHA3; ISSN: 0021-9258  
AU Yokoyama, H.; Nakayama, T. O. M.; Chichester, C. O.  
AN 1962:405959 HCAPLUS  
DN 57:5959  
OREF 57:1273b-e
- L246 ANSWER 211 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Natural [poly(**isoprenyl**)]phenols. **Synthesis** of  
grifolin and ostruthin  
SO Gazzetta Chimica Italiana (1969), 99(3), 308-15  
CODEN: GCITA9; ISSN: 0016-5603  
AU Cardillo, Giuliana; Cricchio, Renato; Merlini, Lucio; Nasini, Gianluca  
AN 1969:422201 HCAPLUS  
DN 71:22201
- L246 ANSWER 212 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Function of sterols in Mycoplasma  
SO Abhandlungen der Deutschen Akademie der Wissenschaften zu Berlin, Klasse  
für Medizin (1969), Volume Date 1968, No. 2, 37-45  
CODEN: ADWMAX; ISSN: 0568-4250  
AU Smith, Paul Francis  
AN 1969:457813 HCAPLUS  
DN 71:57813
- L246 ANSWER 213 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Radioisotopic studies on the biosynthesis of the glyceryl diether lipids  
of Halobacterium cutirubrum  
SO Canadian Journal of Biochemistry (1968), 46(8), 971-7  
CODEN: CJBIAE; ISSN: 0008-4018  
AU Kates, M.; Wassef, M. K.; Kushner, D. J.  
AN 1968:457576 HCAPLUS  
DN 69:57576
- L246 ANSWER 214 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Biosynthesis of N6-( $\Delta^2$ -isopentenyl)adenosine. Precursor relation of  
**acetate** and mevalonate to the  $\Delta^2$ -isopentenyl group of the  
transfer ribonucleic acid of microorganisms  
SO Biochemistry (1968), 7(3), 940-4  
CODEN: BICHAW; ISSN: 0006-2960  
AU Fittler, Fritz; Kline, Larry K.; Hall, Ross Hume  
AN 1968:84264 HCAPLUS  
DN 68:84264
- L246 ANSWER 215 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Effect of previous illumination time of etiolated leaves of Spirodela  
polyrrhiza on the radioactivity in **carotenoids**, due to sodium  
**acetate**-2- $^{14}\text{C}$ , incorporation in the dark  
SO Comptes Rendus des Seances de l'Academie des Sciences, Serie D: Sciences  
Naturelles (1968), 267(7), 733-6  
CODEN: CHDDAT; ISSN: 0567-655X  
AU Moneger, Rene  
AN 1969:896 HCAPLUS  
DN 70:896
- L246 ANSWER 216 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Biosynthesis of .beta.-**carotene** from one-carbon units  
SO Pharmazie (1968), 23(10), 594  
CODEN: PHARAT; ISSN: 0031-7144  
AU Reichel, Ludwig; Schreiber, Gerhard

AN 1969:17697 HCAPLUS  
DN 70:17697

L246 ANSWER 217 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Effect of light on **carotenoid** biosynthesis in *Spirodela*  
*polyrrhiza*  
SO Physiologie Vegetale (1968), 6(2), 165-202  
CODEN: PHYVAP; ISSN: 0031-9368  
AU Moneger, Rene  
AN 1968:457482 HCAPLUS  
DN 69:57482

L246 ANSWER 218 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Secondary **carotenoids** in green algae. I. Chemistry,  
occurrence, and factors controlling the biogenesis of these polyenes  
SO (1968), 61(1), 81-102  
AU Czygan, Franz C.  
AN 1968:93812 HCAPLUS  
DN 68:93812

L246 ANSWER 219 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Thermal decomposition of trimethylethylene glycol acetates  
SO Azerbaidzhanskii Khimicheskii Zhurnal (1968), (1), 61-3  
CODEN: AZKZAU; ISSN: 0005-2531  
AU Movsumzade, M. M.; Ismailova, F. E.  
AN 1968:486231 HCAPLUS  
DN 69:86231

L246 ANSWER 220 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Purification of waste water in the first step of **isoprene**  
**synthesis** from isobutylene and formaldehyde  
SO U.S.S.R.  
From: Izobret., Prom. Obraztsy, Tovarnye Znaki 1967, 44(6), 188.  
CODEN: URXXAF  
IN Zheleznyak, A. S.; Nemtsov, M. S.; Ogorodnikov, S. K.; Lesteva, T. M.;  
Pokorskii, V. N.; Trenke, K. M.; Shapiro, L. P.; Yablochkina, M. N.  
AN 1968:81248 HCAPLUS  
DN 68:81248

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	SU 193367		19670302	SU	19640603

L246 ANSWER 221 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI 4-Hydroxyretinal  
SO Fr., 3 pp.  
CODEN: FRXXAK  
IN Reedy, Albert J.  
AN 1968:29903 HCAPLUS  
DN 68:29903

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 1484573		19670609		

L246 ANSWER 222 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Cyclization of dehydroneerolidol **acetate** as a route to the  
**synthesis** of cyclic **isoprenoids**  
SO Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya (1967), (5), 1144-6  
CODEN: IASKA6; ISSN: 0002-3353  
AU Semenovskii, A. V.; Smit, V. A.; Chernova, T. N.; Kucherov, V. F.  
AN 1968:2997 HCAPLUS  
DN 68:2997

L246 ANSWER 223 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Bacterial **carotenoids**. XXIII. **Carotenoids** of



- Thiorhodaceae. 6. Total **synthesis** of okenone and related compounds
- SO Acta Chemica Scandinavica (1947-1973) (1967), 21(4), 970-82  
 CODEN: ACSAA4; ISSN: 0001-5393
- AU Aasen, Arne J.; Liaaen Jensen, Synnoeve  
 AN 1967:473716 HCAPLUS  
 DN 67:73716
- L246 ANSWER 224 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Effect of dietary cholesterol and ubiquinone on **isoprene synthesis** in rat liver
- SO Archives of Biochemistry and Biophysics (1967), 121(1), 147-53  
 CODEN: ABBIA4; ISSN: 0003-9861
- AU Krishnaiah, K. V.; Joshi, V. C.; Ramasarma, T.  
 AN 1967:451879 HCAPLUS  
 DN 67:51879
- L246 ANSWER 225 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Biological activity of **carotenoids** in the bird
- SO Zentralblatt fuer Veterinaermedizin, Reihe A (1967), 14(2), 119-28  
 CODEN: ZVRAAX; ISSN: 0300-8711
- AU Prohaszka, Laszlo; Toth, Marton  
 AN 1967:419023 HCAPLUS  
 DN 67:19023
- L246 ANSWER 226 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Telomerization reaction of **isoprene** with acetic acid
- SO Eesti NSV Teaduste Akadeemia Toimetised, Keemia, Geoloogia (1967), 16(1), 37-47  
 CODEN: EKEGAI; ISSN: 0424-6373
- AU Erm, A.; Laats, K.  
 AN 1967:490950 HCAPLUS  
 DN 67:90950
- L246 ANSWER 227 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Mechanism of diene C<sub>5</sub>H<sub>8</sub> (**isoprene**) **production** in illuminated leaves
- SO Fiziologiya Rastenii (Moscow) (1966), 13(5), 753-61  
 CODEN: FZRSAY; ISSN: 0015-3303
- AU Sanadze, G. A.  
 AN 1967:8846 HCAPLUS  
 DN 66:8846
- L246 ANSWER 228 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Influence of lipid components of Mycoplasma laidlawii membranes on osmotic fragility of cells
- SO Journal of Bacteriology (1966), 91(2), 609-16  
 CODEN: JOBAAY; ISSN: 0021-9193
- AU Razin, S.; Tourtellotte, M. E.; McElhaney, R. N.; Pollack, J. D.  
 AN 1966:53896 HCAPLUS  
 DN 64:53896  
 OREF 64:10115b-d
- L246 ANSWER 229 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Role of **carotenoids** in egg **production** and in the liveability of baby chicks
- SO Magyar Allatorvosok Lapja (1966), 21(12), 552-5  
 CODEN: MGALA5; ISSN: 0025-004X
- AU Prohaszka, Laszlo; Toth, Marton  
 AN 1967:83546 HCAPLUS  
 DN 66:83546
- L246 ANSWER 230 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI **Synthesis** in the **carotenoids** series. XX. Novel

**syntheses** of apocarotenoids  
SO Helvetica Chimica Acta (1966), 49(1), 369-90  
CODEN: HCACAV; ISSN: 0018-019X  
AU Schwieter, U.; Gutmann, H.; Lindlar, H.; Marret, R.; Rigassi, N.; Ruegg, R.; Schaeren, S. F.; Isler, O.  
AN 1966:68009 HCAPLUS  
DN 64:68009  
OREF 64:12734b-h,12735a-d

L246 ANSWER 231 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Syntheses** of **carotenoidal** compounds. II. Preparation of polyene(benzo)fulvenes  
SO Recueil des Travaux Chimiques des Pays-Bas (1966), 85(3), 339-42  
CODEN: RTCPA3; ISSN: 0165-0513  
AU Haeck, H. H.; Kralt, T.  
AN 1966:420974 HCAPLUS  
DN 65:20974  
OREF 65:3915g-h,3916a-c

L246 ANSWER 232 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Biogenesis of **carotenoids** in Trentepohlia aurea  
SO Zeitschrift fuer Pflanzenphysiologie (1966), 55(1), 59-64  
CODEN: ZSPPAD; ISSN: 0044-328X  
AU Czygan, Franz Christian; Kalb, Klaus  
AN 1966:475605 HCAPLUS  
DN 65:75605  
OREF 65:14151e-f

L246 ANSWER 233 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Contemporary notions on the biosynthesis of **carotenoids**  
SO Ukrain'skii Botanichnii Zhurnal (1966), 23(2), 3-11  
From: Ref. Zh., Biol. Khim. 1967, Abstr. No. 2F803  
CODEN: UKBZAW; ISSN: 0372-4123  
AU Drokova, G.  
AN 1967:112109 HCAPLUS  
DN 66:112109

L246 ANSWER 234 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Quaternary ionylidenethylphosphonium salts  
SO 11 pp.  
IN Nuerrenbach, Axel; Sarnecki, Wilhelm; Reif, Werner  
AN 1965:498600 HCAPLUS  
DN 63:98600  
OREF 63:18156c-f

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 1395458	----	19650409	-----	-----

L246 ANSWER 235 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Xanthonenes. VI. Claisen rearrangements, selective demethylations, and synthesis of dihydroisojacareubin and alvaxanthone trimethyl ether  
SO Tetrahedron (1965), 21(9), 2653-69  
CODEN: TETRAB; ISSN: 0040-4020  
AU Burling, E. D.; Jefferson, A.; Scheinmann, F.  
AN 1965:498140 HCAPLUS  
DN 63:98140  
OREF 63:18011a-h,18012a-e

L246 ANSWER 236 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Carotenoids** and related compounds. XI. **Syntheses** of .delta.-**carotene** and .epsilon.-**carotene**  
SO Journal of the Chemical Society, Abstracts (1965), (March), 2019-26  
CODEN: JCSAAZ; ISSN: 0590-9791  
AU Manchand, P. S.; Ruegg, R.; Schwieter, U.; Siddons, P. T.; Weédon, B. C.

L.  
AN 1965:74391 HCAPLUS  
DN 62:74391  
OREF 62:13187b-d

L246 ANSWER 237 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Comparative biosynthesis of mevalonic acid by Mycoplasma  
SO Journal of Bacteriology (1965), 89(1), 146-53  
CODEN: JOBAAY; ISSN: 0021-9193  
AU Smith, Paul F.; Henrikson, C. V.  
AN 1965:24065 HCAPLUS  
DN 62:24065  
OREF 62:4353e-g

L246 ANSWER 238 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Vitamin A and **isoprenoid synthesis** in the rat  
SO Biochemical Journal (1965), 95(1), 138-43  
CODEN: BIJOAK; ISSN: 0264-6021  
AU Diplock, A. T.; Green, J.; Bunyan, J.  
AN 1965:61219 HCAPLUS  
DN 62:61219  
OREF 62:10899c-d

L246 ANSWER 239 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI The lipase and pigments of staphylococci  
SO Annals of the New York Academy of Sciences (1965), 128(1), 132-51  
CODEN: ANYAA9; ISSN: 0077-8923  
AU Stewart, Gordon T.  
AN 1965:501202 HCAPLUS  
DN 63:101202  
OREF 63:18681b-d

L246 ANSWER 240 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Biosynthesis of ubiquinone (coenzyme Q) in microorganisms  
SO Bulletin of the National Institute of Sciences of India (1965), No. 28,  
25-31  
CODEN: BNSIAE; ISSN: 0027-9528  
AU Jayaraman, J.; Raman, Tarakad S.  
AN 1967:26725 HCAPLUS  
DN 66:26725

L246 ANSWER 241 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Syntheses** of .beta.-**carotene** and **lycopene**  
from 4-octene-2,7-dione  
SO Justus Liebig's Annalen der Chemie (1965), 684, 14-24  
CODEN: JLACBF; ISSN: 0075-4617  
AU Kabbe, Hans Joachim; Truscheit, Ernst; Eiter, Karl  
AN 1965:431860 HCAPLUS  
DN 63:31860  
OREF 63:5688e-h,5689a-c

L246 ANSWER 242 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Carotenoids** and related compounds. XII. **Synthesis** of  
chlorobactene, "HO-chlorobactene" and rhodopin  
SO Acta Chemica Scandinavica (1964), 18(7), 1739-44  
CODEN: ACHSE7; ISSN: 0904-213X  
AU Bonnett, R.; Spark, A. A.; Weedon, B. C. L.  
AN 1965:439278 HCAPLUS  
DN 63:39278  
OREF 63:7052f-h,7053a-e

L246 ANSWER 243 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI 3-Methyl-3-buten-1-ol **acetate** and **isoprene** glycol  
diacetate

SO 3 pp.  
AN 1963:415164 HCAPLUS  
DN 59:15164  
OREF 59:2653h,2654a

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 918962		19630220	GB	

L246 ANSWER 244 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Vitamin A intermediates

SO 6 pp.

IN Truscheit, Ernst; Eiter, Karl; Oediger, Hermann; Stein, Eberhard; Kabbe, Hans J.; Lorenz, Rudolf

AN 1963:468787 HCAPLUS

DN 59:68787

OREF 59:12661f-h,12662a

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 1149353		19630530	DE	19600803
	GB 952498			GB	
	US 3247239		1966	US	

L246 ANSWER 245 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Asymmetrical incorporation of **acetate**-14C into .beta.-

**carotene** bio-**synthesized** by *Phycomyces blakesleeanus*

SO Proceedings of the Society for Experimental Biology and Medicine (1963), 114, 444-7

CODEN: PSEBAA; ISSN: 0037-9727

AU Lotspeich, F. J.; Krause, R. F.; Lilly, V. G.; Barnett, H. L.

AN 1964:32973 HCAPLUS

DN 60:32973

OREF 60:5916g-h

L246 ANSWER 246 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI The incorporation of C14O2 **acetate**-2-C14, and mevalonate-2-C14 into the **carotenoids** of mature tomato leaves

SO Ann. Physiol. Vegetale (1963), 5(2), 115-40

AU Costes, C.

AN 1963:464175 HCAPLUS

DN 59:64175

OREF 59:11895g-h,11896a

L246 ANSWER 247 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Action of diterpene alcohols on the biosynthesis of **carotenoids** and phytol, using **acetate**-2-C14 in maize plantules

SO Compt. Rend. (1962) 355-7

AU Costes, Claude

AN 1962:485298 HCAPLUS

DN 57:85298

OREF 57:17082h-i

L246 ANSWER 248 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI The effect of diphenylamine on **carotenoid**, sterol, and fatty acid **synthesis** in *Phycomyces blakesleeanus*

SO Archives of Biochemistry and Biophysics (1962), 97, 138-45

CODEN: ABBIA4; ISSN: 0003-9861

AU Olson, James Allen; Knizley, Homer, Jr.

AN 1962:412893 HCAPLUS

DN 57:12893

OREF 57:2657c-e

L246 ANSWER 249 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Partial **syntheses** of **carotenes** by means of lead tetraacetate

SO Rev. Chim., Acad. Rep. Populaire Roumaine (1962), 7(1), 79-84  
AU Bodea, C.; Nicoara, E.  
AN 1963:435760 HCAPLUS  
DN 59:35760  
OREF 59:6450f-h

L246 ANSWER 250 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Improvement in synthesis of vitamin A acid and related compounds  
IN Pommer, Horst; Sarnecki, Wilhelm  
AN 1962:67055 HCAPLUS  
DN 56:67055  
OREF 56:12960g-i,12961a-i,12962a-i,12963a,12964a  
PATENT NO. KIND DATE APPLICATION NO. DATE  
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PI US 3006939 19611031 US

L246 ANSWER 251 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Influence of insect lures on hyphal growth and sporulation of Choanephora trispora  
SO Canadian Journal of Microbiology (1961), 7, 807-13  
CODEN: CJMIAZ; ISSN: 0008-4166  
AU Zajic, James E.; Kuehn, H. H.  
AN 1962:33992 HCAPLUS  
DN 56:33992  
OREF 56:6468c-f

L246 ANSWER 252 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Mevalonic acid and **carotenogenes** in carrot extracts  
SO Naturwissenschaften (1961), 48, 738-9  
CODEN: NATWAY; ISSN: 0028-1042  
AU Modi, V. V.; Patwa, D. K.  
AN 1962:80803 HCAPLUS  
DN 56:80803  
OREF 56:15806f-g

L246 ANSWER 253 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Acetate** incorporation into the **carotenoids** of Chromatium  
SO Biochimica et Biophysica Acta (1961), 54, 525-32  
CODEN: BBACAQ; ISSN: 0006-3002  
AU Benedict, C. R.; Fuller, R. C.; Bergeron, J. A.  
AN 1962:55919 HCAPLUS  
DN 56:55919  
OREF 56:10683h-i

L246 ANSWER 254 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Glucose as a carbon source for **carotene synthesis** in tomatoes  
SO Archives of Biochemistry and Biophysics (1961), 93, 231-7  
CODEN: ABBIA4; ISSN: 0003-9861  
AU Purcell, Albert E.; Thompson, Guy A., Jr.  
AN 1961:112745 HCAPLUS  
DN 55:112745  
OREF 55:21255c-e

L246 ANSWER 255 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Factors affecting the **production** of **carotene** by Choanephora cucurbitarum  
SO Mycologia (1961), Volume Date 1960, 52, 80-96  
CODEN: MYCOAE; ISSN: 0027-5514  
AU Chu, F. S.; Lilly, Virgil Greene  
AN 1962:55975 HCAPLUS  
DN 56:55975  
OREF 56:10696b-f

L246 ANSWER 256 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Enzymic **synthesis** of **carotenoids** in cell-free extracts  
of carrot  
SO Enzymologia (1961), 23, 27-34  
CODEN: ENZYAS; ISSN: 0013-9424  
AU Modi, V. V.; Patwa, D. K.  
AN 1961:100109 HCAPLUS  
DN 55:100109  
OREF 55:18888e

L246 ANSWER 257 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI .gamma.,.gamma.-Dimethylallyl **acetate**  
IN Samokhvalov, G. I.; Miropol'skaya, M. A.; Fedotova, N. I.; Anosov, V. I.;  
Nashatyrev, A. N.; Savostin, A. P.  
AN 1960:80369 HCAPLUS  
DN 54:80369  
OREF 54:15248g-i

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI SU 125800		19600201	SU	

L246 ANSWER 258 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Enzymic **synthesis** and destruction of **carotenoids** in  
mango extracts  
SO Experientia (1960), 16, 352  
CODEN: EXPEAM; ISSN: 0014-4754  
AU Modi, V. V.; Patwa, D. K.  
AN 1961:23351 HCAPLUS  
DN 55:23351  
OREF 55:4663a-b

L246 ANSWER 259 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Carotenoid syntheses**. XXVIII. **Syntheses** of  
4-hydroxy derivatives of .beta.-apocarotenals and .beta.-apocarotenic  
acids as well as the preparation of 3,4-dehydro-.beta.-apocarotenals and  
3,4-dehydro-.beta.-apocarotenic acids  
SO Helvetica Chimica Acta (1960), 43, 94-101  
CODEN: HCACAV; ISSN: 0018-019X  
AU Entschel, R.; Karrer, P.  
AN 1961:131429 HCAPLUS  
DN 55:131429  
OREF 55:24822b-f

L246 ANSWER 260 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI The **production** of **carotene** by Phycomyces  
blakesleeana. II. The **production** of radioactive .beta.-  
**carotene** by using Phycomyces blakesleeana  
SO West Va., Univ. Agr. Expt. Sta., Bull. (1960), No. 441T, 61-76  
From: Biol. Abstr. 35, Abstr. No. 64209(1960).  
AU Lilly, Virgil Greene; Barnett, H. L.; Krause, R. F.  
AN 1961:138181 HCAPLUS  
DN 55:138181  
OREF 55:26134i,26135a-b

L246 ANSWER 261 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Synthesis** of oxygenated **carotenoids**  
SO Voprosy Khim. Terpenov i Terpenoidov; Akad. Nauk Litovsk. S.S.R., Trudy  
Vsesoyuz. Soveshchaniya, Vil'nyus (1960), Volume Date 1959 43-9  
AU Samokhvalov, G. I.; Vakulova, L. A.  
AN 1961:93066 HCAPLUS  
DN 55:93066  
OREF 55:17490g-i

- L246 ANSWER 262 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Carotenogenesis**. XXVI. The incorporation of **acetate**  
-C14, mevalonate-C14 and C14O2 into **.beta.-carotene** by the  
fungus *Phycomyces blakesleeana*  
SO Biochemical Journal (1960), 76, 5-10  
CODEN: BIJOAK; ISSN: 0264-6021  
AU Braithwaite, G. D.; Goodwin, T. W.  
AN 1960:130324 HCAPLUS  
DN 54:130324  
OREF 54:25062f-h
- L246 ANSWER 263 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Carotenogenesis**. XXV. The incorporation of **acetate**  
-1-C14, **acetate**-2-C14 and C14O2 into **lycopene** by  
tomato slices  
SO Biochemical Journal (1960), 76, 1-5  
CODEN: BIJOAK; ISSN: 0264-6021  
AU Braithwaite, G. D.; Goodwin, T. W.  
AN 1960:130323 HCAPLUS  
DN 54:130323  
OREF 54:25062d-f
- L246 ANSWER 264 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Biosynthesis of **carotenes** in carrot extracts  
SO Nature (London, United Kingdom) (1959), 184(Suppl. No.13), 983-4  
CODEN: NATUAS; ISSN: 0028-0836  
AU Modi, V. V.; Patwa, D. K.  
AN 1960:63306 HCAPLUS  
DN 54:63306  
OREF 54:12276c-d
- L246 ANSWER 265 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Syntheses** in the **carotenoid** series. XV.  
**Syntheses** in the **.beta.**, **carotenal** and **.beta.-**  
**carotenol** series  
SO Helvetica Chimica Acta (1959), 42, 854-64  
CODEN: HCACAV; ISSN: 0018-019X  
AU Ruegg, R.; Montavon, M.; Ryser, G.; Saucy, G.; Schwieter, U.; Isler, O.  
AN 1960:2428 HCAPLUS  
DN 54:2428  
OREF 54:625b-i
- L246 ANSWER 266 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Comparison of the incorporation of labeled CO<sub>2</sub>, **acetate** and  
mevalonate into **carotenoids** in a number of **carotenogenic**  
systems  
SO C I B A Foundation Symposium Biosynthesis of Terpenes and Sterols (1959),  
Volume Date 1958 279-91, discussion 291-4  
AU Goodwin, T. W.  
AN 1960:17695 HCAPLUS  
DN 54:17695  
OREF 54:3602d-i,3603a
- L246 ANSWER 267 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Biosynthesis of **carotenoids** by microorganisms  
SO Ciba Foundation Symposium Biosynthesis of Terpenes and Sterols (1959),  
Volume Date 1958 267-76, discussion 277-8  
AU Grob, E. C.  
AN 1960:29345 HCAPLUS  
DN 54:29345  
OREF 54:5810a-d
- L246 ANSWER 268 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **.beta.-Carotene** fermentation

SO Rept. Taiwan Sugar Expt. Sta. (Taiwan) (1959), 20, 91-100  
From: Biol. Abstr. 36, Abstr. No. 18343(1961).  
AU Su, K. C.  
AN 1962:471698 HCAPLUS  
DN 57:71698  
OREF 57:14290a-c

L246 ANSWER 269 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Thermal rearrangement of ergosterol peroxide  
SO Ann. (1959), 620, 46-62  
AU Bergmann, Werner; Meyers, Martin B.  
AN 1959:112015 HCAPLUS  
DN 53:112015  
OREF 53:20132i,20133a-i,20134a

L246 ANSWER 270 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Carotenoid syntheses**. XXIV. Further reactions of  
.beta.- and .alpha.-**carotene** with bromosuccinimide  
SO Helvetica Chimica Acta (1958), 41, 983-7  
CODEN: HCACAV; ISSN: 0018-019X  
AU Entschel, R.; Karrer, P.  
AN 1958:113912 HCAPLUS  
DN 52:113912  
OREF 52:20234h-i,20235a-b

L246 ANSWER 271 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Carotenogenesis**. XXV. The incorporation of C14-carbon dioxide,  
**acetate**-C14, and mevalonate-C14 into .beta.-**carotene** by  
illuminated etiolated maize seedlings  
SO Biochemical Journal (1958), 70, 612-17  
CODEN: BIJOAK; ISSN: 0264-6021  
AU Goodwin, T. W.  
AN 1959:12402 HCAPLUS  
DN 53:12402  
OREF 53:2367c-f

L246 ANSWER 272 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Carotenoid** biosynthesis in tomatoes  
SO Proceedings of the American Society for Horticultural Science (1958), 71,  
349-55  
CODEN: PASHA6; ISSN: 0099-4065  
AU Francis, F. J.  
AN 1958:105417 HCAPLUS  
DN 52:105417  
OREF 52:18692i,18693a-b

L246 ANSWER 273 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI The chemical mechanism of acetoacetic acid synthesis in the liver  
SO Biochemische Zeitschrift (1958), 330, 269-95  
CODEN: BIZEA2; ISSN: 0366-0753  
AU Lynen, Feodor; Henning, Ulf; Bublitz, Clark; Sorbo, Bo; Kroplin-Rueff,  
Luistraud  
AN 1961:60388 HCAPLUS  
DN 55:60388  
OREF 55:11586a-e

L246 ANSWER 274 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Effect of light and temperature on the **production** of  
**carotenoid** pigments by + and - sexes of *Phycomyces blakes-leeanus*  
SO Proc. West Va. Acad. Sci. (1958), Volume Date 1957-1958, 29/30, 25-31  
AU Lilly, V. G.; Barnett, H. L.; Krause, R. F.  
AN 1960:23855 HCAPLUS  
DN 54:23855  
OREF 54:4771g-i,4772a



L246 ANSWER 275 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Unsaturated compounds

AN 1958:6619 HCAPLUS

DN 52:6619

OREF 52:1223i,1224a-c

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI GB 775060		19570515	GB	
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US 2917539		1959	US	
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L246 ANSWER 276 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Total **synthesis** of **isoprenoid** alcohols

SO Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya (1957) 1267-70  
CODEN: IASKA6; ISSN: 0002-3353

AU Nazarov, I. N.; Gusev, B. P.; Gunar, V. I.

AN 1958:34658 HCAPLUS

DN 52:34658

OREF 52:6150h-i,6151a-g

L246 ANSWER 277 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI **Syntheses** in the **carotenoid** series. VIII. Total **synthesis** of cryptoxanthin and a further synthesis of zeaxanthin

SO Helv. Chim. Acta (1957), 40, 456-67

AU Isler, O.; Lindlar, H.; Montavon, M.; Ruegg, R.; Saucy, G.; Zeller, P.

AN 1957:62225 HCAPLUS

DN 51:62225

OREF 51:11293i,11294a-f

L246 ANSWER 278 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Xanthinin, a monocarbocyclic sesquiterpenoid lactone

SO Chem. & Ind. (London) (1957) 328

AU Geissman, T. A.; Deuel, P. G.

AN 1957:62224 HCAPLUS

DN 51:62224

OREF 51:11293f-i

L246 ANSWER 279 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Biosynthesis of polyisoprenoids. I. Synthesis of .beta.-hydroxy-.beta.-methylglutaric acid semialdehyde

SO Ann. (1957), 608, 71-8

AU Eggerer, Hermann; Lynen, Feodor; Rauenbusch, Erich; Kessel, Ingrid

AN 1958:77035 HCAPLUS

DN 52:77035

OREF 52:13633h-i,13634a-d

L246 ANSWER 280 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Metabolism of **acetate** in Hevea brasiliensis

SO Nature (London, United Kingdom) (1957), 180, 37

CODEN: NATUAS; ISSN: 0028-0836

AU Patrick, A. D.

AN 1958:73021 HCAPLUS

DN 52:73021

OREF 52:13012a-c

L246 ANSWER 281 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Mevalonic acid and **carotenogenesis** in Phycomyces blakesleeianus

SO Biochemical Journal (1957), 66, 31P-32P

CODEN: BIJOAK; ISSN: 0264-6021

AU Braithwaite, G. D.; Goodwin, T. W.

AN 1959:23880 HCAPLUS

DN 53:23880

OREF 53:4430a-c

L246 ANSWER 282 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Polyene diether acetals and their manufacture and conversion into polyene aldehydes  
 AN 1957:30032 HCAPLUS  
 DN 51:30032  
 OREF 51:5835b-f

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 753635		19560725	GB	

L246 ANSWER 283 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI 2,7-Dimethyl-2,6-octadien-4-yne-1,8-dial  
 AN 1956:89478 HCAPLUS  
 DN 50:89478  
 OREF 50:16862a-b

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 744890		19560215	GB	

L246 ANSWER 284 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI The synthesis and configuration of neo-b vitamin A and neoretinene b  
 SO Journal of the American Chemical Society (1956), 78, 2651-2  
 CODEN: JACSAT; ISSN: 0002-7863  
 AU Oroshnik, Wm.  
 AN 1956:81938 HCAPLUS  
 DN 50:81938  
 OREF 50:15467h-i,15468a-c

L246 ANSWER 285 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI The biosynthesis of .beta.-**carotene** by Mucor hiemalis. IV. The part played by acetic acid in the **synthesis** of the **carotene** molecule, especially positions 3,4,6 and 3',4',6', studied with the aid of carbon 14-labeled acetic acid  
 SO Helv. Chim. Acta (1956), 39, 1975-80  
 AU Grob, E. C.; Butler, R.  
 AN 1957:17881 HCAPLUS  
 DN 51:17881  
 OREF 51:3741h-i

L246 ANSWER 286 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI **Carotenogenesis**. XVIII. **Carotenoid production** by a strongly chromogenic bacterium isolated from butter  
 SO Biochemical Journal (1956), 62, 275-81  
 CODEN: BIJOAK; ISSN: 0264-6021  
 AU Goodwin, T. W.; Jamikorn, Malini  
 AN 1956:40957 HCAPLUS  
 DN 50:40957  
 OREF 50:7935c-f

L246 ANSWER 287 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI **Syntheses** in the **carotenoid** series. II. **Synthesis** of various ring components  
 SO Helvetica Chimica Acta (1956), 39, 259-73  
 CODEN: HCACAV; ISSN: 0018-019X  
 AU Isler, O.; Montavon, M.; Ruegg, R.; Zeller, P.  
 AN 1956:81940 HCAPLUS  
 DN 50:81940  
 OREF 50:15468h-i,15469a-i,15470a-b

L246 ANSWER 288 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Some new aspects of acetic acid involved in biosynthesis of .beta.-**carotene**  
 SO Chimia (Switz.) (1956), 10, 258-9  
 AU Grob, E. C.; Butler, R.

AN 1957:91830 HCAPLUS  
DN 51:91830  
OREF 51:16696b-d

L246 ANSWER 289 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI **Syntheses** in the **carotenoid** series. XXXIV.  
**Syntheses** of C14- and C15-aldehydes

SO Ann. (1956), 598, 51-64

AU Inhoffen, Hans Herloff; Erdmann, Dietrich

AN 1956:81949 HCAPLUS

DN 50:81949

OREF 50:15474c-i,15475a-f

L246 ANSWER 290 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI An alternate fatty acid cycle involving thioesters of pantetheine

SO Journal of the American Chemical Society (1955), 77, 5194-5

CODEN: JACSAT; ISSN: 0002-7863

AU Stern, Joseph R.

AN 1956:5051 HCAPLUS

DN 50:5051

OREF 50:1107b-c

L246 ANSWER 291 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI The biosynthesis of .beta.-**carotene** by *Mucor hiemalis*. The use of acetic acid in the **synthesis** of the **carotene** molecule, especially in positions 14-15, 14'-15' and 10-11, 10'-11', investigated with C14-acetic acid. III

SO Helvetica Chimica Acta (1955), 38, 1313-16

CODEN: HCACAV; ISSN: 0018-019X

AU Grob, E. C.; Butler, R.

AN 1955:78595 HCAPLUS

DN 49:78595

OREF 49:14904d-f

L246 ANSWER 292 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI **Carotenogenesis**. XV. The role of carboxylic acids in the biosynthesis of .beta.-**carotene** by *Phycomyces blakesleeanus*

SO Biochemical Journal (1955), 60, 649-55

CODEN: BIJOAK; ISSN: 0264-6021

AU Friend, J.; Goodwin, T. W.; Griffiths, L. A.

AN 1955:78514 HCAPLUS

DN 49:78514

OREF 49:14886e-h

L246 ANSWER 293 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI Evaluation of methyl esters, by-product of the extraction of **carotene** from palm oil

SO Oleagineux (1955), 10, 99-105, 193-6, 269-73

CODEN: OLEAAF; ISSN: 0030-2082

AU Jorand, J.

AN 1955:72026 HCAPLUS

DN 49:72026

OREF 49:13670e-g

L246 ANSWER 294 OF 324 HCAPLUS COPYRIGHT 2003 ACS

TI **Carotenogenesis**. **Synthesis** of .beta.-methylcrotonic acid by *Phycomyces blakesleeanus*

SO Proceedings of the International Congress of Biochemistry (1955) 87

CODEN: 18USAR

AU Goodwin, T. W.; Modi, V. V.

AN 1956:74532 HCAPLUS

DN 50:74532

OREF 50:14052g-i

- L246 ANSWER 295 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Synthesis** of polyenes. VI. **Isoprenoid** polyenes  
containing sterically hindered cis configurations  
SO Journal of the American Chemical Society (1954), 76, 5719-36  
CODEN: JACSAT; ISSN: 0002-7863  
AU Oroshnik, Wm.; Mebane, Alexander D.  
AN 1955:77776 HCAPLUS  
DN 49:77776  
OREF 49:14702g-i,14703a-i,14704a-i,14705a-i,14706a-b
- L246 ANSWER 296 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI The biosynthesis of .beta.-**carotene** by *Mucor hiemalis*. The use  
of acetic acid in the **synthesis** of the **carotene**  
molecule, especially the ionone grouping, investigated with C14-acetic  
acid. II  
SO Helvetica Chimica Acta (1954), 37, 1908-12  
CODEN: HCACAV; ISSN: 0018-019X  
AU Grob, E. C.; Butler, R.  
AN 1955:12636 HCAPLUS  
DN 49:12636  
OREF 49:2567g-i
- L246 ANSWER 297 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI The exchange of **carotenoids** in higher plants  
SO Zeitschrift fuer Botanik (1954), 42, 387-435  
CODEN: ZBOTA3; ISSN: 0372-8102  
AU Beekmann, Helga  
AN 1955:33015 HCAPLUS  
DN 49:33015  
OREF 49:6396f-i
- L246 ANSWER 298 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI The effect of pantothenic acid, pantethine, and phosphorylated pantethine  
on **carotenoid** formation by *Mucor hiemalis*  
SO Experientia (1954), 10, 378-9  
CODEN: EXPEAM; ISSN: 0014-4754  
AU Grob, E. C.; Grundbacher, V.; Schopfer, W. H.  
AN 1955:5037 HCAPLUS  
DN 49:5037  
OREF 49:1113e-f
- L246 ANSWER 299 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI The biosynthesis of .beta.-**carotene** by *Mucor hiemalis*. The use  
of acetic acid in the **synthesis** of the **carotene**  
molecule investigated with C14-labeled acetic acid  
SO Experientia (1954), 10, 250-1  
CODEN: EXPEAM; ISSN: 0014-4754  
AU Grob, E. C.; Butler, R.  
AN 1954:60664 HCAPLUS  
DN 48:60664  
OREF 48:10796g-h
- L246 ANSWER 300 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Studies of cholesterol biosynthesis. II. Distribution of **acetate**  
carbon in the ring structure  
SO Biochemical Journal (1953), 54, 597-601  
CODEN: BIJOAK; ISSN: 0264-6021  
AU Cornforth, J. W.; Hunter, G. D.; Popjak, G.  
AN 1953:66351 HCAPLUS  
DN 47:66351  
OREF 47:11279a-c
- L246 ANSWER 301 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI The biosynthesis of **carotenoids** by *Phycomyces blakesleeana*

SO Internationale Zeitschrift fuer Vitaminforschung (1952), 23, 484-9  
 CODEN: IZVIAK; ISSN: 0020-9406  
 AU Grob, E. C.; Schopfer, W. H.; Poretti, G. G.  
 AN 1952:54871 HCAPLUS  
 DN 46:54871  
 OREF 46:9156h-i

L246 ANSWER 302 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Biosynthesis of **carotenoids**  
 SO Biochemische Zeitschrift (1952), 323, 376-81  
 CODEN: BIZEA2; ISSN: 0366-0753  
 AU Arnaki, M.; Sary, Z.  
 AN 1953:29064 HCAPLUS  
 DN 47:29064  
 OREF 47:4951b-d

L246 ANSWER 303 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI **Carotenogenesis** in *Phycomyces blakesleeana*  
 SO Congres International de Biochimie, Resumes des Communications (1952) 210  
 CODEN: 20DPAQ  
 AU Goodwin, T. W.; Griffiths, L. A.; Jamikorn, Malini; Willmer, J. S.  
 AN 1956:1924 HCAPLUS  
 DN 50:1924  
 OREF 50:436c-d

L246 ANSWER 304 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI **Syntheses** in the **carotenoid** series. XXIV. Attempts to  
 prepare 3,3',4,4'-bisdehydro-.beta.-**carotene**  
 SO Ann. (1952), 578, 177-87  
 AU Inhoffen, Hans H.; Arend, Wolfgang  
 AN 1954:3541 HCAPLUS  
 DN 48:3541  
 OREF 48:652f-i,653a-g

L246 ANSWER 305 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI The **synthesis** of .beta.-**carotene** by *Phycomyces*  
 cultured in a medium containing sodium **acetate** as the only  
 source of carbon  
 SO Experientia (1952), 8, 140  
 CODEN: EXPEAM; ISSN: 0014-4754  
 AU Shopfer, W. H.; Grob, E. C.  
 AN 1952:67547 HCAPLUS  
 DN 46:67547  
 OREF 46:11310c-d

L246 ANSWER 306 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI Investigation of the biosynthesis of **carotenoids** by *Sarcina*  
*lutea*  
 SO Folia Pharmaceutica (Istanbul) (1952), 2, 115-18  
 CODEN: FOPMAS; ISSN: 0428-8300  
 AU Arnaki, M.; Sary, Z.  
 AN 1953:29088 HCAPLUS  
 DN 47:29088  
 OREF 47:4955a-c

L246 ANSWER 307 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
 TI The preparation of cyclic vinyl ethers  
 SO Journal of the American Chemical Society (1951), 73, 913-14  
 CODEN: JACSAT; ISSN: 0002-7863  
 AU Parham, Wm. E.; Holmquist, Howard E.  
 AN 1951:46987 HCAPLUS  
 DN 45:46987  
 OREF 45:7998c-g

L246 ANSWER 308 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI The mechanism of rubber formation in the guayule. III. Experiments with isotopic carbon  
SO Archives of Biochemistry and Biophysics (1951), 31, 234-47  
CODEN: ABBIA4; ISSN: 0003-9861  
AU Arreguin, Barbarin; Bonner, James; Wood, Betty Jean  
AN 1951:31405 HCAPLUS  
DN 45:31405  
OREF 45:5439a-c

L246 ANSWER 309 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI The **production** of marked .beta.-**carotene** by Phycomyces blakesleeana  
SO Experientia (1951), 7, 218-19  
CODEN: EXPEAM; ISSN: 0014-4754  
AU Grob, E. C.; Poretti, G. G.; von Muralt, A.; Schopfer, W. H.  
AN 1952:3039 HCAPLUS  
DN 46:3039  
OREF 46:568a-b

L246 ANSWER 310 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Ethyl sorbate in the diene synthesis  
SO Journal of the American Chemical Society (1949), 71, 2865-8  
CODEN: JACSAT; ISSN: 0002-7863  
AU Rigg, M. Wesley; Rosenthal, Rudolph  
AN 1951:5236 HCAPLUS  
DN 45:5236  
OREF 45:892c-h

L246 ANSWER 311 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Synthesis** of **isoprenoid** compounds in plants  
SO Journal of Chemical Education (1949), 26, 628-31  
CODEN: JCEDA8; ISSN: 0021-9584  
AU Bonner, James  
AN 1950:17984 HCAPLUS  
DN 44:17984  
OREF 44:3576b-d

L246 ANSWER 312 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Syntheses** in the **carotenoid** series. II.  
**Synthesis** of a hydrocarbon, C<sub>30</sub>H<sub>42</sub>  
SO Ann. (1948), 561, 26-31  
AU Inhoffen, Hans H.; Pommer, Horst; Bohlmann, Ferdinand  
AN 1949:13106 HCAPLUS  
DN 43:13106  
OREF 43:2588d-i

L246 ANSWER 313 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Effect of various salts on the **synthesis** of ascorbic acid and **carotene** in cress seedlings  
SO Biochem. J. (1947), 41, 197-205  
AU Mapson, L. W.; Cruickshank, E. M.  
AN 1948:2878 HCAPLUS  
DN 42:2878  
OREF 42:644h-i,645a

L246 ANSWER 314 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Synthesis** of aliphatic terpene alcohols from **isoprene**  
SO Ber. (1943), 76B, 831-46  
AU Lennartz, Theo.  
AN 1944:11772 HCAPLUS  
DN 38:11772  
OREF 38:1737g-i,1738a-i,1739a

L246 ANSWER 315 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Syntheses** in the **carotenoid** series. V. Preparation of  
higher aliphatic polyenealdehydes  
SO Ann. (1941), 547, 285-02  
AU Schmitt, J.; Obermeit, A.  
AN 1942:41253 HCAPLUS  
DN 36:41253  
OREF 36:6523g-h

L246 ANSWER 316 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Syntheses** in the **carotenoid** series. IV. Preparation of  
.omega.-phenyl-and .omega.-furylpolyenealdehydes  
SO Ann. (1941), 547, 270-84  
AU Schmitt, J.  
AN 1942:41252 HCAPLUS  
DN 36:41252  
OREF 36:6523e-g

L246 ANSWER 317 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Syntheses** in the **carotenoid** series. III. Preparation  
of a methyl homolog of dehydro-.beta.-cyclocitral  
SO Ann. (1941), 547, 256-70  
AU Schmitt, J.  
AN 1942:41251 HCAPLUS  
DN 36:41251  
OREF 36:6522i,6523a-e

L246 ANSWER 318 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Synthesis** of terpenes from **isoprene**  
SO Ann. (1932), 496, 52-77  
AU Wagner-Jauregg, T.  
AN 1932:41789 HCAPLUS  
DN 26:41789  
OREF 26:4320h-i,4321a-b

L246 ANSWER 319 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI Synthetic experiments with ethynylcarbinols. I. Transformation of  
3-methyl-butinol into 3-methylbutenin, 3-methylbutanolone and its  
condensation products  
SO Ber. (1922), 55B, 2903-23  
AU Scheibler, Helmut; Fischer, Artur  
AN 1923:8065 HCAPLUS  
DN 17:8065  
OREF 17:1419b-i,1420a-b

L246 ANSWER 320 OF 324 HCAPLUS COPYRIGHT 2003 ACS  
TI **Making isoprene**  
IN Webel, F.  
AN 1914:19261 HCAPLUS  
DN 8:19261  
OREF 8:2816d-e

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 1098859		19140602	US	

L246 ANSWER 321 OF 324 NTIS COPYRIGHT 2003 NTIS  
TI Biosynthesis of Membrane Lipids in Halobacterium Cutirubrum.  
Reprint: Biosynthesis of Membrane Lipids in Halobacterium Cutirubrum.  
NR AD-679 417/XAB; NRC-10141  
9p; 1968  
AU Kates, M.; Wassef, M. K.; Kushner, D. J.  
AN 1969(31):02662 NTIS

L246 ANSWER 322 OF 324 WPIDS (C) 2003 THOMSON DERWENT

TI **Prodn of isoprene.**

PI JP 46000161 B (197102)\*

L246 ANSWER 323 OF 324 WPIDS (C) 2003 THOMSON DERWENT

TI Quat phosphonium salts as intermediates for **carotenoids**.

PI GB 1102064 A (196800)\*

NL 6704300 A (196801)

US 3517067 A (197025)

L246 ANSWER 324 OF 324 WPIDS (C) 2003 THOMSON DERWENT

TI 3-methyl-but-2-en-1-ol or 3-methyl-but-2-en-1-yl.

PI BE 725088 A (196800)\*

NL 6817562 A (196801)

CA 833592 A (197006)

FR 1594968 A (197042)

GB 1239434 A (197127)

DE 1643709 B (197128)

US 3655735 A (197218)

CH 525173 A (197237)

JP 48007408 B (197310)

=> save temp l246 lycopene/a

ANSWER SET L246 HAS BEEN SAVED AS 'LYCOPENE/A'

=> d ab 19,25,33-35,40,41,115,116,267

L121 ANSWER 19 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AB The invention is concerned with a multi-stage process for **making** an oxidative metabolite of the **carotenoid lycopene**, 2,6-cyclolycopene-1,5-diol having the formula ##STR1## In this process alpha-terpinyl **acetate** is oxidatively dihydroxylated to a cyclohexanediol (IV), the cyclohexanediol (IV) is oxidatively cleaved to a ketoaldehyde (V), the ketoaldehyde (V) is subjected to an intramolecular aldol condensation to give a cyclopentanol (VI), the cyclopentanol (VI) is silylated to its silylated derivative formylcyclopentane (VII), the formylcyclopentane (VII) is subjected to a C3 -chain lengthening with acetone and simultaneously to a saponification for the cleavage of the acetyl group to give a cyclopentylbutenone (VIII), the cyclopentylbutenone (VIII) is reacted with vinyl magnesium bromide to give a pentadienol (IX), the pentadienol (IX) is converted with deprotection of the silylated hydroxy group into a phosphonium salt (X), this salt is subjected to a Wittig reaction with 2,7-dimethyl-2,4,6-octatriene-1,8-dial to give a tridecahexaenal (XII) and the tridecahexaenal (XII) is subjected to a Wittig reaction with a (3,7,11-trimethyl-dodeca-2,4,6,10-tetraenyl)triphenylphosphonium salt to give the desired 2,6-cyclolycopene-1,5-diol (II). A variant of this process, also in accordance with the invention, comprises converting the cyclopentylbutenone (VIII) into the phosphonium salt (X) via two alternative intermediates, namely a pentadienoic acid ester (XIV) and a different pentadienol (XV), into the same phosphonium salt (X). Moreover, the invention is concerned with the novel intermediates (V), (VI), (VII), (VIII), (IX), (X), (XII), (XIV) as well as (XV) and the individual process steps which lead to these novel intermediates. 2,6-cyclolycopene-1,5-diol is useful in the prevention of cancer growth in human cells.

L121 ANSWER 25 OF 324 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 12

AB In summary the biosynthetic pathway for the formation of **isoprenoid** compounds in plants is similar to the pathway of sterol biosynthesis in animals and yeast. In plants, **isoprenoids** are **synthesized** from acetyl-CoA via mevalonate and isopentyl pyrophosphate to long-chain prenyl pyrophosphates. These compounds may then be metabolized to form various **isoprenoid** compounds. The bovine corpus luteum, which utilizes the Porter-Lincon pathway, has been



shown to metabolize **acetate** to steroids and **.beta.-carotene**. For example, farnesyl pyrophosphate is an intermediate in the **production** of steroids and **.beta.-carotene**. The **synthesis** of **carotenoids** continues with the condensation of two molecules of geranylgeranyl pyrophosphate to phytoene (C40 hydrocarbon), phytofluene, and eventually to **.beta.-carotene**. **.beta.-Carotene** can then be metabolized to retinol. Retinol is important for the synthesis of cholesterol and the metabolism of various steroids, such as pregnenolone and progesterone. The action of vitamin A on progesterone metabolism is important for embryonic development.

L121 ANSWER 33 OF 324 HCAPLUS COPYRIGHT 2003 ACS

AB A review with 17 refs. on the novel 1-deoxy-D-xylulose-5-phosphate (DOXP) pathway of isopentenyl diphosphate (IPP) formation, which is located in plastids. Higher plants and several algae groups possess a dichotomy in their **isoprenoid** biosynthesis, whereby their plastidic **isoprenoids** are **synthesized** via the novel DOXP pathway. However, their cytosolic sterols are formed via the cytosolic **acetate**/mevalonate pathway of IPP formation. Various mono- and diterpenes are also formed via the plastidic DOXP pathway. Apparently, the DOXP pathway is present in all oxygen-evolving photosynthetic organisms. Data indicate that the prokaryotic chloroplasts as endosymbionts conserved their former bacterial DOXP pathway of IPP formation which appears to be as old as the **acetate**/mevalonate pathway that has been found in other bacterial groups.

L121 ANSWER 34 OF 324 MEDLINE DUPLICATE 16

AB For many years it was accepted that isopentenyl diphosphate, the common precursor of all **isoprenoids**, was **synthesized** through the well known **acetate**/mevalonate pathway. However, recent studies have shown that some bacteria, including *Escherichia coli*, use a mevalonate-independent pathway for the synthesis of isopentenyl diphosphate. The occurrence of this alternative pathway has also been reported in green algae and higher plants. The first reaction of this pathway consists of the condensation of (hydroxyethyl)thiamin derived from pyruvate with the C1 aldehyde group of D-glyceraldehyde 3-phosphate to yield D-1-deoxyxylulose 5-phosphate. In *E. coli*, D-1-deoxyxylulose 5-phosphate is also a precursor for the biosynthesis of thiamin and pyridoxol. Here we report the molecular cloning and characterization of a gene from *E. coli*, designated *dxs*, that encodes D-1-deoxyxylulose-5-phosphate synthase. The *dxs* gene was identified as part of an operon that also contains *ispA*, the gene that encodes farnesyl-diphosphate synthase. D-1-Deoxyxylulose-5-phosphate synthase belongs to a family of transketolase-like proteins that are highly conserved in evolution.

L121 ANSWER 35 OF 324 HCAPLUS COPYRIGHT 2003 ACS

AB Isopentenyl diphosphate, the common precursor of all **isoprenoids**, has been widely assumed to be synthesized by the **acetate**/mevalonate pathway in all organisms. However, based on in vivo feeding expts., isopentenyl diphosphate formation in several eubacteria, a green alga, and plant chloroplasts has been demonstrated very recently to originate via a mevalonate-independent route from pyruvate and glyceraldehyde 3-phosphate as precursors. Here we describe the cloning from peppermint (*Mentha x piperita*) and heterologous expression in *Escherichia coli* of 1-deoxy-D-xylulose-5-phosphate synthase, the enzyme that catalyzes the first reaction of this pyruvate/glyceraldehyde 3-phosphate pathway. This synthase gene contains an ORF of 2,172 base pairs. When the proposed plastid targeting sequence is excluded, the deduced amino acid sequence indicates the peppermint synthase to be about 650 residues in length, corresponding to a native size of roughly 71 kDa. The enzyme appears to represent a novel class of highly conserved transketolases and likely plays a key role in the biosynthesis of plastid-derived **isoprenoids** essential for growth, development, and defense in plants.

L121 ANSWER 40 OF 324 MEDLINE DUPLICATE 18

AB Labeling experiments using [1-13C]**acetate** or [1-13C]glucose were performed with opportunistic pathogenic bacteria, with innocuous bacteria related to pathogenic species or with phytopathogenic species. The labeling pattern was determined in the **isoprenic** moiety of ubiquinone or menaquinone derivatives. These experiments showed that *Acinetobacter*, *Citrobacter*, *Erwinia*, *Pseudomonas*, *Burkholderia*, *Ralstonia* and *Mycobacterium* **synthesize** their **isoprenoids** via the mevalonate-independent glyceraldehyde 3-phosphate/pyruvate route. Enzymes of this novel bacterial metabolic route, which is apparently absent in vertebrates and man, therefore represent potential targets for a novel type of antibacterial drugs.

L121 ANSWER 41 OF 324 HCAPLUS COPYRIGHT 2003 ACS

AB Factors affecting manuf. of **carotenoids** with photosynthetic *Rhodospseudomonas* sp. R-41. The yield of **carotenoid** was increased from 23.8 mg/g dry cell to 57.3 mg/g dry cell under the optimal conditions: **acetate** as C source, Na glutamate N source, yeast exts. growth factors, Mg<sup>2+</sup> 4 mg/L, Fe<sup>3+</sup> 2 mg/L, 1500 lx and incubation at 30.degree., micro-aerobic for 120 h.

L121 ANSWER 115 OF 324 HCAPLUS COPYRIGHT 2003 ACS

AB Wild-type *P. blakesleeanus* **synthesizes** the yellow pigment, .beta.-**carotene**. Color mutants exhibit various alterations in the biosynthesis of .beta.-**carotene** or in its regulation. The presence of certain chems. in the medium stimulates **carotenogenesis** in the wild type. Different mechanisms of action are attributed to agents which stimulate or fail to stimulate different sets of mutants; this is the case of retinol and di-Me phthalate. Di-Me phthalate and veratrol are active on the same mutants, and therefore are likely to act in the same way. The main regulation of **carotenogenesis**, end-product inhibition, does not operate in the mutants of certain genes; these mutants are indifferent to retinol. By using a collection of retinoids it was concluded that their action depends on their structural similarity to a part of the .beta.-**carotene** mol. These and other observations suggest that end-product inhibition of the pathway is mediated by a complex of .beta.-**carotene** and two gene products and that the retinoids compete with .beta.-**carotene** and prevent end-product inhibition.

L121 ANSWER 116 OF 324 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. DUPLICATE 50

AB Carefully isolated intact spinach chloroplasts virtually free of contamination of other organelles effectively form .beta.-**carotene** from NaH<sup>14</sup>CO<sub>3</sub> or [U-14C]-3-phosphoglycerate (PGA) under photosynthetic conditions. The photosynthate pool formed in chloroplasts from 1 to 2 millimolar [U-14C]-3-PGA or 3 to 6 millimolar NaH<sup>14</sup>CO<sub>3</sub> was fully sufficient to supply .beta.-**carotene synthesis** with intermediates for about 1 hour at maximal rates of about 20 nanomoles <sup>14</sup>C incorporated per milligram chlorophyll per hour. Fatty acid synthesis remains, under these circumstances, in linear dependence to substrate concentrations with far lower activity. Isotopic dilution of the .beta.-**carotene synthesis** by adding unlabeled glyceraldehyde 3-phosphate, dihydroxyacetone-P, 3-PGA, 2-PGA, phosphoenolpyruvate, pyruvate, respectively, may be interpreted as a direct substrate flow from photosynthetically fixed CO<sub>2</sub> to isopentenyl pyrophosphate synthesizing system. Unlabeled **acetate** did not dilute .beta.-**carotene synthesis**. Fatty acid **synthesis** acted similarly with unlabeled substrates; but it also was diluted by unlabeled **acetate**. These results indicate a tight linkage of photosynthetic carbon fixation and plastid **isoprenoid synthesis**.

L121 ANSWER 267 OF 324 HCAPLUS COPYRIGHT 2003 ACS

AB Microorganisms including numerous molds produce **carotenoids** from **acetate** and mevalonic acid. *Phycomyces blakesleeana* and *Mucor hiemalis*, produce **carotenoid** as the principal substance. **Carotenogenesis** is induced by different carbohydrates, fatty acids, acids of the citric acid cycle, and pyruvic acid. With C14-**acetate** both C atoms of HOAc are incorporated into **.beta.-carotene**. The labeling pattern of **.beta.-carotene** conforms with that of squalene. With these microorganisms the **synthesis** of sterols and **carotenoids** runs parallel, suggesting a common **isoprenoid** precursor. Coenzyme A influences the formation of precursor as biosynthesis is increased by pantothenic acid, pantetheine and phosphorylated pantetheine which are essential constituents of coenzyme A. Mevalonic acid must be considered as the active or at least as related to the active **isoprenoid** precursor. C40 **carotenoids** are composed of 8 molecules of mevalonic acid. The C40 analog of squalene is lycopersene. The proposed pathway: tetrahydrolycopene, **lycopene** and **.beta.-carotene** is confirmed for this biosynthesis. The first **carotenoid** is **lycopene** and this is recognized as the precursor of all **carotenoids**. The pathway is **lycopene**, **.gamma.-carotene**, **.beta.-carotene**, **.psi.-carotene**-epoxide and mutachrome. *Neurospora crassa* grows in the dark with no **carotenoid** production, but upon exposure to light rapidly forms **carotenoids**. Cultures grown in the dark in a N atm. do not produce **carotenoid** until O is introduced. In the dark, more satd. **carotenoids** form in *N. crassa* indicating that **.psi.-carotene** and neurosporene are immediate precursors of **lycopene**. In 6 hrs. **.delta.-** and **.gamma.-carotene** appear. **.gamma.-Carotene** probably is derived from **lycopene** by ring closure. It is possible that **carotenoids** hydroxylated in the 3 or 3' positions derive from a colorless polyene.

=> log y

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
39.67	39.88

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-3.26	-3.26

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